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No. XIII. OF VOL. I., 1940. LONDON, SATURDAY, MARCH 30, 1940. Pp. 96—Price 1s.
No. 6083. VOL. CCXXXVIII. Founded 1823. PUBLISHED WEEKLY. Registered as a Newspaper. Annual Subscription: Inland £2 2s. Abroad £2 10s.

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ADDRESSES AND ORIGINAL ARTICLES

LUPUS ERYTHEMATOSUS*
THE EFFECTS OF SULPHONAMIDES

By H. W. Barber, M.B. Camb., F.R.C.P.
PHYSICIAN IN CHARGE OF THE SKIN DEPARTMENT AT GUY'S HOSPITAL, LONDON

A brief reference (Barber 1938) has previously been made to the effects of sulphanilamide in lupus erythematosus. In many instances this disease appears to respond in a peculiar way to sulphonamides, and enough cases have now been observed to have enabled me several times to forecast with accuracy the train of events that would follow the administration of these drugs. My experience during the last twenty years has strengthened my tentative suggestion (Barber 1915) that, whereas in some cases the eruption may be a toxi-tuberculide, it may sometimes be a cutaneous reaction to acute or chronic streptococcal infection and possibly to other infections. I now believe that most cases met with in this country, except, possibly, in certain areas where tuberculosis is prevalent, are of streptococcal origin; but this is not necessarily true of other countries. It is probable that further investigations, employing the pathogen method of bacterial culture, will confirm this view.

INVESTIGATION

I have used sulphonamides in lupus erythematosus and many other diseases, acute and chronic, for about two and a half years. Nearly all my observations concern Prontosil Album and Dagenan (M. & B. 693).† I have also prescribed Rubiazol for a few patients with lupus erythematosus in whom the other two drugs repeatedly caused severe reactions. Most of the patients were investigated to determine whether tuberculous, streptococcal, or other chronic infections were present. In the few in whom tuberculosis appeared likely to be responsible for the eruption the reactions to be described did not take place after administration of prontosil or of dagenan, nor was the eruption benefited. One of these has been observed recently. The patient, a middle-aged man, has had the disease for several years. The active eruption, which involves chiefly the face, is of the indolent indurated type, with hyperkeratosis, and has left deep scars where it has cleared. It is in this type of eruption that I always suspect a tuberculous origin. Investigations did not reveal any focus of streptococcal infection, except some infected teeth, but a radiogram of the chest showed evidence of tuberculosis of the bronchial glands, with calcareous nodules and dense surrounding fibrosis. Intracutaneous tests were strongly positive to tuberculin and negative to streptococcal emulsion. Three dagenan tablets a day were given for three weeks. They caused no reaction, nor did they visibly affect the eruption.

In most cases a chronic and often widespread streptococcal infection was found. When obvious foci of such infection were present—e.g., infected teeth or tonsils—these were removed before treatment with sulphonamides began. This is an important point, for it is unlikely that the drugs could have any permanent effect on grossly infected foci. In some cases, however, no accessible foci were discovered, but the patients gave a history of the previous removal of such foci or of acute diseases presumably streptococcal in origin, such as recurrent tonsillitis, scarlet fever, or rheumatic fever.

REACTIONS TO PRONTOSIL AND TO DAGENAN

Reactions to initial treatment.—After receiving either prontosil or dagenan for eight to fourteen days most patients began to feel acutely ill, and the temperature rose, sometimes after an initial rigor. In some cases a generalised scarlatiniform eruption appeared. This eruption I regard as due to the liberation of streptococcal toxin by the drug from latent foci of infection. It differs from the other types of eruption which may be provoked by these drugs and in some instances appear to be due to the production of porphyrin with consequent photosensitivity. So far as I know, in no case did this scarlatiniform erythema recur after subsequent administration of the drug. In several patients focal reactions in the patches of lupus erythematosus developed, the eruption becoming more inflamed and sometimes swollen. In one patient even minute doses of dagenan, and to a less extent of prontosil, always caused erythematous haloes to appear round the patches, with scattered areas on the limbs of an erythema which subsided with desquamation. The reactions in several patients were accompanied, apart from general malaise, by severe rheumatic pains, and in some by swelling and tenderness of lymphatic glands. As a rule, when the reactions developed, the drug was discontinued, and the symptoms rapidly subsided.

Reactions to subsequent treatment.—In some cases a single tablet, or even a quarter of one, has caused within a short time (an hour or less) severe reactions with rise of temperature and sometimes a rigor. In others, although reactions have developed either immediately or after a while, they have gradually diminished in intensity until the patient has been able to take the drug with no ill effects. Even one of my most sensitive patients, in whom at one time the taking of a quarter of a tablet of dagenan caused a violent reaction, both general and focal, with rigor and high fever, was able after a while to tolerate short courses of small doses with great benefit. In a few patients, one of whom had the acute disseminated form of the disease and eventually died of pneumonia, the reactions were so severe that it was thought inadvisable, or the patient refused, to continue the treatment.

Therapeutic effect.—On the whole this has been good, sometimes strikingly so. Some patients had previously had prolonged treatment with gold salts or with bismuth, and they declared that the effects of prontosil or of dagenan were incomparably superior to those of other treatments. On the other hand, I cannot yet say how permanent the results will be, and several patients relapsed after their lesions had entirely or partially disappeared.

Nature of reactions.—In no other diseases that I have treated with prontosil or with dagenan have I observed reactions at all comparable with those which have developed with remarkable uniformity in lupus erythematosus. It may be argued that they are merely examples of those described by Hageman and Blake (1937) and Long and Bliss (1939) as drug fever. Admittedly the usual interval between the beginning of treatment and the occurrence of the fever are about the same in both types of reaction, and in both the

* An expanded version of this paper will appear in the *British Journal of Dermatology and Syphilis*.
† I am indebted to Messrs. May and Baker for supplying me with this drug.

fever and other symptoms subside soon after the drug is omitted, but there are several points which render it unlikely that they are of identical origin. These may be summarised as follows:—

(1) *Percentage incidence.*—Hageman and Blake observed drug fever in 15·6 per cent. of cases, and Long and Bliss in 9 per cent. of adults and 3 per cent. of children. Out of eleven cases of lupus erythematosus selected without reference to their occurrence febrile reactions of varying severity were observed in eight—i.e., in 72·7 per cent. In patients treated by me with the sulphonamides for diseases other than lupus erythematosus the percentage incidence of fever has been even lower than that recorded by the above authors. If the reactions described in lupus erythematosus were due to drug fever their high percentage incidence would suggest that patients with this disease are abnormally liable to become sensitised to these drugs; but this is a priori unlikely, and, although many patients appear peculiarly vulnerable to the effects of an acute infection, other drugs, such as quinine, the salicylates, iodine, arsenic, gold and bismuth, are usually well tolerated by them.

(2) *General symptoms.*—In my cases of lupus erythematosus these were not only more severe but differed in kind from those described in drug fever. Widespread fibromuscular pains were an almost constant feature, and in those who had suffered from arthritis there were usually swelling and pain in the affected joints. In several patients there was enlargement and tenderness of lymphatic glands. Hageman and Blake state that swelling of the joints or glands were never observed in their cases of drug fever, and fibromuscular pains are not mentioned either by them or by Long and Bliss.

(3) *Eruptions.*—Of the various types of eruption that may apparently be provoked by the sulphonamides a morbilliform erythema is admittedly the commonest. Apart from a coincident purpura in one case and urticaria in another, it was the only one observed by Hageman and Blake, and appeared in nine of their twenty-one cases of drug fever. In my cases of lupus erythematosus it was never seen, although it may possibly have occurred in ambulatory patients whom I was unable to observe at the time of their reactions. On the other hand a widespread scarlatiniform erythema has appeared during the early stages of the reaction in several cases, but to my knowledge has never recurred when the drug has been readministered. It is significant that this should have been the only generalised eruption observed in my cases, and in my opinion it is more likely that liberation of streptococcal toxin was responsible for it rather than the drug itself. The most striking cutaneous manifestation, however, has been the focal reactions in the patches of lupus erythematosus. I am satisfied that these were not the result of "protein-shock" for reasons that I cannot discuss here.

(4) *Readministration of the drug.*—Long and Bliss in some of their cases of drug fever have noted an immediate febrile reaction, sometimes accompanied by "an erysipeloid œdematous lesion" of the face, when the drug was readministered. Some of my patients with lupus erythematosus, who had had severe febrile reactions with their first course of treatment, again reacted severely even after taking one tablet or less, this reaction exactly resembling the first, but in the majority the reactions rapidly diminished, and—an important point—there was then not only improvement in the eruption but also often a disappearance of accompanying symptoms such as rheumatic pains.

(5) *Drug sensitivity.*—In some cases symptoms referable to the drug have arisen, such as gastro-intestinal disturbances, ulcers in the mouth, urticaria, swelling of the face, pins-and-needles in the extremities, and, in one case, severe neuritic pain, but these differed from the reactions described, and, moreover, reappeared with the same severity whenever an attempt was made to readminister the drug. In one case the patient became sensitive to dagenan, but can take prontosil, which originally caused febrile reactions, without ill effects.

Mode of action of sulphonamide compounds.—In spite of much research by many workers the exact mode of action of these drugs upon bacteria is not yet fully understood. It seems clear that they destroy the capsules of the organisms and prevent their formation, and that they favour effective phagocytosis. In my previous communication upon the action of prontosil album on a facial carbuncle (Barber 1938) I expressed the view that the severe febrile reaction that occurred within a few hours of taking the drug could only be explained on the assumption that the drug caused a liberation of bacterial toxin. This view has been supported by recent observations on a case of widespread afebrile erysipelas. In neither case could the reactions observed be due to drug fever. In the same way I regard the febrile reactions that I have observed in some patients with lupus erythematosus treated with sulphonamide compounds as due not directly to the drug but to the liberation of bacterial toxins—streptococcal toxin in these cases—by the action of the drug on latent foci of infection. This view accords with, and appears to be the only likely explanation of, the clinical facts observed:—

(1) The appearance in some cases of a generalised scarlatiniform erythema at the time of the first febrile reaction.

(2) The occurrence in some patients of swelling and tenderness of the lymphatic glands, which doubtless represent secondary foci of infection.

(3) The occurrence of focal reactions in the eruption sometimes with the development of a transitory erythema round the patches.

(4) The temporary exacerbation of rheumatic pains in the fibromuscular tissues and in the joints in those already suffering from fibrositis or from arthritis.

(5) The diminution—gradual or relatively rapid—of the reactions on further administration of the drug. It is clear that, if the reactions are provoked by destruction of bacteria in latent foci of infection, they will naturally diminish as fewer and fewer bacteria remain.

(6) The improvement in or the disappearance of the eruption and of other symptoms, such as rheumatism, with the continued administration of the drug.

Influence of focal infection.—I wish to emphasise a point which, if my view of the action of these drugs is correct, the above observations teach us—namely, the importance of latent subsidiary foci of infection in the mucosæ of the upper respiratory tract and intestines, in the lymphatic glands, and doubtless in other tissues, such as the fibromuscular system. One of the chief arguments against the influence of focal infection in the ætiology of certain diseases has been the disappointing results that so often accrue from the removal or treatment of accessible foci of infection. These are generally admitted, and I think it will be agreed that the more long-standing the disease the more disappointing, as a rule, is the result. I have always held that a partial explanation, at any rate, may be that in chronic cases subsidiary foci of infection persist after the more obvious ones have been dealt with.

Moreover, in certain chronic diseases, although infection may have been the primary cause, its persistence has produced such profound effects on the tissues and the endocrine-sympathetic system that complete recovery is impossible. On the other hand, we all have experience of recent cases of arthritis or other conditions in which removal of an infective focus has

led to an immediate and dramatic cure, and I have seen this happen several times in lupus erythematosus, when the duration of the disease was a matter of weeks or months and not, as is so often the case, of years. The undoubted value of sulphonamides in those long-standing cases of lupus erythematosus in which I have thought a chronic and widespread streptococcal invasion to be responsible is that at long last they afford us a method of attacking latent and inaccessible foci of infection.

Relation to causal organism.—I have already said that in a few patients with lupus erythematosus in whom I thought chronic tuberculosis was responsible these drugs produced neither reactions nor any therapeutic effect. It might be argued nevertheless that my results with other cases do not necessarily indicate that the infection responsible was streptococcal, and I agree. Those, for example, who have suggested that the disease is due to an unknown specific organism might ascribe the therapeutic effects of the drugs to their action on such an organism. The hypothetical organism in question, however, would presumably be a filtrable virus or possibly a protozoon. In this connexion I may mention that the sulphonamides appear to have some therapeutic influence on pemphigus and a very evident one on dermatitis herpetiformis, which is, like pemphigus, considered by some to be caused by a virus. In none of the cases of these diseases that I have treated with prontosil or with dagenan has there been any reaction of the kind that I have described in lupus erythematosus, although there may have been slight symptoms of drug-intolerance.

TREATMENT

Apart from the serious and sometimes fatal effects that may follow the administration of the sulphonamides even in moderate dosage, the severity of the reactions that often result from their use in lupus erythematosus makes it imperative that they should be given with the greatest discretion. The patient should always be warned that such reactions are likely to develop, and that the drug should be omitted at once when the preliminary symptoms arise. When the eruption is acute and widespread, ambulatory treatment should never be attempted, and the patient should rest in bed for several days before beginning a course of the drug, and in all cases gross foci of infection should first be dealt with. It cannot be too strongly emphasised that the indiscriminate use of the sulphonamides is fraught with danger. As regards dosage I prescribe seldom more than one tablet thrice daily, and often less.

ILLUSTRATIVE CASE-RECORD

The following severe case, which was recently seen in consultation with Dr. Justina Wilson and will be published in full later, is an example of the effects of sulphonamides when a chronic streptococcal infection is present and apparently responsible for the eruption. The patient was investigated thoroughly, and, although they were probably not the main source of infection, three teeth were extracted before treatment with dagenan was begun.

A woman, aged 56 and rather obese, had had arthritis of her knees and severe fibrositis and had been subject to attacks of cystitis, tonsillitis, and urticaria. The lupus erythematosus first appeared in June, 1939, and, when seen by me early in the following November, was severe and widespread. There were large symmetrical patches involving the greater parts of the cheeks, one on either side of the nose, one over each eyebrow, and several on the forehead, backs of the hands and forearms, and legs. The eruption was intensely congested and threatened to become of the acute disseminated type that so often ends fatally.

The patient was put completely at rest in bed in a nursing-home, and, after the investigations were completed and the infected teeth extracted, dagenan was prescribed. On the first day (Nov. 29) two tablets were given, and then three a day until Dec. 10—i.e., thirty-five tablets were taken in twelve days. Towards the end of this period there were considerable gastro-intestinal discomfort and much intestinal flatulence. On the 10th the patient felt cold and shivered, and the temperature rose to 100·2° F. in the evening but fell the next day when she took two more tablets. On the morning of the 12th it rose to 99° F., and later to 100·2° F., and two tablets were given during the day. On the morning and evening of the 13th the temperature rose again to 100·2° F., and no tablets were taken. The following day it fell to subnormal and remained so. This febrile reaction was accompanied by severe and generalised muscular pains, a scarlatiniform erythema involving chiefly the trunk and limbs, and an intense focal reaction in the lupus erythematosus. On the 13th, the last day of the pyrexia, the large patches on the cheeks had extended and had become confluent with those on the nose, forming the complete "butterfly" or "bat's wing" erythema. All the patches on the face and limbs were intensely congested and several, which had almost faded, were again actively inflamed.

When I saw her again six days later, the reaction had entirely subsided, and all the patches on the arms except two had faded, those on the face had flattened down and were for the most part now merely "stains," and the recent erythematous patches, which had caused those on the cheeks and nose to become confluent, had disappeared. The patient felt well and a few days later returned home.

She was seen again on Jan. 8, 1940, when she looked and felt extremely well. There were slightly active remains of the patches on the cheeks and over the left eyebrow, but the rest of the eruption had disappeared except for slight staining in certain areas.

It is probable that there will be some relapse, and that further courses of dagenan will be necessary, but for the present it has been decided to continue with the vaccine prepared by Dr. John Bodman from the strains of streptococci isolated by the pathogen-selection method and to keep the patient under observation.

This was one of the cases in which, after I had received the results of the investigations, I was able to predict with accuracy the train of events that would follow the administration of dagenan. In a case of this type I believe (1) that the presence of active patches of lupus erythematosus is evidence that the patient is absorbing streptococcal toxin or antigen from, as a rule, multiple foci of infection; (2) that prontosil and dagenan either directly or indirectly destroy the streptococci in the various foci and liberate toxin which provokes the complex reaction described. This consists of a rise of temperature, usually preceded by a rigor of varying intensity; generalised or localised pains in the fibromuscular tissues; a widespread scarlatiniform erythema; a focal reaction in existing patches of the eruption, reactivation of healed patches, and the appearance of new erythematous lesions continuous with or distinct from areas already affected; and painful swelling of lymphatic glands when these are subsidiary foci of infection; (3) that when the reaction has subsided, improvement or disappearance of the eruption takes place owing to diminished absorption of toxin or antigen; and (4) that, although subsequent administration of the drug may be followed by an immediate and severe reaction, possibly owing to the remaining organisms being more vulnerable or accessible to it, the reactions tend progressively to diminish as the organisms are gradually destroyed.

SUMMARY

1. It is suggested that lupus erythematosus may be either of tuberculous or streptococcal origin.

2. When the disease has been apparently due to streptococcal infection, characteristic reactions to treatment with the sulphonamides have been observed, with subsequent benefit to the eruption, in a high proportion of cases, whereas when a tuberculous infection was apparently responsible these reactions have not occurred, nor has the eruption been affected.

3. The view is put forward that these reactions are due to the liberation of streptococcal toxin by the action of the sulphonamides on latent foci of infection and are not examples of drug fever.

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THE MYSTERY OF ALIMENTATION

By E. P. Cathcart, C.B.E., M.D. Glasg., F.R.S.
REGIUS PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF GLASGOW.

II

How much protein should the average adult diet contain? This is a subject which, in the past at least, has led to acute controversy. The figure suggested by Voit of approximately 118 g. a day was as a rule favoured by the older investigators, but within recent years it has been generally accepted that this figure is too high. The Technical Commission on Nutrition of the League of Nations suggested that an allowance of 1 g. per kg. of body-weight would suffice. On the basis of Chittenden's and Hindhede's experiments even this allowance is unnecessarily high. It is difficult to decide the point finally, for various "minima" of nitrogen output can be determined. This problem was most ably discussed by von Fürth, who concluded that there were three definite protein minima:—

(1) *The endogenous minimum,* the minimal output of nitrogen in the urine after a period on a protein-free but calorie-rich diet. It is in practice impossible to maintain nitrogen equilibrium at this level, because the output does not represent the total protein metabolism—e.g., resynthesis—which is taking place within the cells. This is indeed a physiological minimum, but it is only of academic interest, although it must remembered that Lusk rightly insisted that "biologically the nitrogen minimum is a protective mechanism of the cells against their destruction."

(2) *The physiological minimum,* which is reached when, with a calorie-rich diet, nitrogen equilibrium can be attained. In practice it means that an intake of 45–60 g. of protein a day will suffice.

(3) *The hygienic or practical minimum,* which is the amount of protein which will suffice to keep the normal man healthy and fit for work. Von Fürth placed this value at 75–90 g. of protein a day. Generally speaking, calories derived from protein should form 10–14 per cent. of the total calories ingested. These and other suggested minima or levels of intake, however, must not be regarded as constants in the physical sense; too many variables can play havoc with their determination and their constancy.

In the establishment of the hygienic or practical minimum, as von Fürth called it, the quality and balance of the diet plays a notable part. This is clear from various experiments. Thus Corry Mann, in an interesting experiment on himself, showed that when he included milk in his diet he could carry on in perfect health on a lower calorie intake than when he used meat as his source of protein. A good deal of evidence suggests that there is a close relation between the katabolism of protein and the calorie intake, a connexion more intimate than merely the katabolism of protein to furnish energy. It has been shown that above a certain relatively low protein intake nitrogen equilibrium on an adequate diet can be readily established. When the subject is underfed—i.e., when the calorie intake is abnormally low—although there may be a fair amount of protein in the diet, this equilibrium cannot be attained; there is a steady loss of nitrogen, a loss which may be even greater than the average loss of nitrogen in complete starvation. Thus, in the personal experiment recorded by Loewy in 1917, when he weighed 51 kg. and was on a diet containing 7–8 g. of absorbable nitrogen with a calorie value varying from 1500 to 1800, his excretion of nitrogen in the urine reached a level of 17 g., approximately 10 g. more than his intake. Levanzin, on the other hand, weighing 47·4 kg. on the thirty-first day of his fast, excreted in his urine only 6·94 g. of nitrogen, just slightly less than he excreted on the first day of his fast. Admittedly these may be extreme examples, but it is an interesting comparison. There is the further interesting point (Benedict) that, when the diet contains an inadequate supply of calories, the loss of nitrogen bears no relation to the enormous reduction in basal metabolism. It is possible that in ordinary feeding, when nitrogen equilibrium can be attained, and in complete starvation, as one of the factors of safety there is a definite anabolic phase of activity, an active resynthesis, whereas in the state of underfeeding the constant but inadequate supply of food may merely stimulate katabolism.

ANABOLISM OF PROTEIN

The anabolic phase of protein metabolism is too often ignored; most of the discussions of metabolism refer to the katabolic phase, which is thus unduly emphasised. Tissue maintenance and growth are discussed, it is true, but the fact that these needs are served by anabolic processes is seldom brought out. Unlike fat and carbohydrate, the amount of true storage of protein, in the adult organism at least, is small; yet there is, as already mentioned, definite evidence that the protein ingested is certainly not immediately katabolised. There is evidence also (Wilson) to suggest, although it would be unwise to dogmatise, that there are two forms of protein retention: (1) a material the composition of which approximates to that of muscle, which is rich in sulphur and is relatively stable, retention taking place apparently when the nitrogen intake is reduced; and (2) a material poor in sulphur, which is relatively unstable and is retained only so long as the nitrogen intake is maintained. The first type of retained protein may be conceived as that which is essential for maintenance and for growth, the second being merely transitional, the type of protein which is rapidly metabolised. If this statement about the type of retention is accepted, it means that the more or less general belief that proteins after ingestion, digestion, and absorption are immediately metabolised in amino-acid form must be reconsidered. It must be remembered, too, that there is evidence that protein can be absorbed from the intestine either unchanged or in complex form.

Too often, implicitly and even explicitly, the metabolism of the various components of the diet, not

merely protein, are believed to undergo individual oxidation. There is some good evidence in favour of the view that the various components are not dealt with separately; indeed, it is more than probable that they become an integral part of the living cell before they undergo the finer series of metabolic changes which lead either to transmutation or destruction. Markowitz and I suggested, from our study of the non-protein R.Q., that it did not represent merely a combustion quotient but was the algebraic sum of the transformations carbohydrate ⇌ fat, plus the oxidation of carbohydrate for energy purposes. The ultimate end may indeed be complete oxidation, but it cannot be accepted that the sole function of the oxygen taken is to bring about combustion in any direct fashion. I still have complete sympathy with Armsby's conception of the metabolic problem:—

"The metabolism of matter and energy in the body might be compared to the exchange of water in a mill pond. The water in the pond may represent the materials of the body itself, while the water running in at the upper end represents the supply of matter and energy in the food, and that going down the flume to the millwheel, the metabolism required for the production of physiological work. . . . The water flowing into the pond does not immediately turn the wheel, but becomes part of the pond and loses its identity. Part of it may be drawn into the main current and enter the flume comparatively soon, while another part may remain in the pond for a very long time."

If we study a chemical factory from the outside, we may determine exactly what goes into the factory; we may also determine the nature of the material which leaves the factory in the form of finished goods and as waste from the chimneys and the sewers; but we may only guess at the various manufacturing processes within the factory.

INTAKE OF PROTEIN AND OUTPUT OF WORK

Another point of considerable interest is that, although commonly there is a definite demand by those who have to carry out hard muscular work for meat (protein in the form of meat), there is no scientific evidence that the body requires an increased intake of protein for this purpose. This demand is made not only by those engaged in productive manual labour but also by the great majority of athletes, as was shown by the investigation of the training diets of some 4700 athletes of over forty races of mankind attending the Olympic games at Berlin in 1936. There is also the evidence that, generally speaking, the more virile races of the world are large consumers of animal protein. Why then does popular demand outrun scientific knowledge? There is no question about the stimulating properties of meat and its extractives; that when it is cooked, particularly when it is roasted or fried, it is tasty and probably directly assists in the increased consumption of food which must be eaten to make good the energy lost. Is it that the diet is not properly balanced, and that the specific dynamic action which then becomes evident, although the energy cannot be utilised for the production of the mechanical work, assists in some as yet unknown fashion? Or is the protein required in larger amount for the maintenance of cell structure, for the eutrophy postulated by Virchow, which occurs during training? Wishart, in his study of the relation of protein intake to the "efficiency" with which prolonged hard muscular work was performed, found that his subject reached his best performance on a high-calorie diet rich in protein of animal origin. He also found, however, that the better performance was not due to the muscular work being carried out more efficiently on the high-protein diets, for the gross efficiency was lower than on diets comparatively poor in protein.

CALCIUM METABOLISM

As the other example of the mystery and difficulties which confront our accurate interpretation of alimentation I have chosen the calcium need. The standards, like those in connexion with total calories and proteins, have fallen with advancing knowledge. Two or three decades ago it was generally held, by Tigerstedt for instance, that the average man required an intake up to 7 g. a day, whereas the commonly accepted Sherman standard postulates a requirement of about 1 g. as optimal for an average adult. What modern work has clearly shown is that it is difficult to speak about the absolute needs for a mineral like calcium, when it can be demonstrated that the need is governed by the amount of phosphorus and vitamin D available. Even in connexion with the phosphorus supply Sherman admits that "there is and can be no one best or most logical ratio. Bone building requires twice as much calcium as phosphorus, whereas cell maintenance requires about twice as much phosphorus as calcium." Our knowledge of calcium needs is strikingly elementary; this is still more true of the other known essential mineral constituents.

Another difficulty which faces us in connexion with the calcium requirements of the body is that the excretion of this material, unlike that of the nitrogen of protein, is mainly in the fæces, only about a quarter to a fifth of the total calcium excreted appearing in the urine. The question at once arises: has all or part or none of the fæcal calcium passed through the metabolic mill in the tissues? Part at least of the material excreted through the intestine has certainly never left the gastro-intestinal tract, having formed compounds which cannot be absorbed.

The mode of excretion has been much discussed in recent years, and the explanatory hypothesis put forward is that a good part at least of the intestinal calcium is absorbed and then excreted into the lumen of the intestine. But there are difficulties in the acceptance of this hypothesis. It has been shown, for example, that a soluble calcium salt, such as the gluconate, injected into the blood-stream causes a definite rise in the output of calcium in the urine and does not influence the intestinal output. There are even graver difficulties. As regards the site of the excretion of the metabolised calcium, the obvious selection of the small intestine was at first made. There is a certain amount of what might be called normal excretion of calcium there, in the various digestive juices; but the experiments of Walsh and Ivy, who found a daily excretion of calcium in the upper jejunum of only 0·32–1·2 mg. and in the lower ileum of 2·0–8·5 mg. suggested that if excretion took place in the small intestine it was but slight. Later Taylor and Fine found that the excretion of calcium in three to five hours from the whole length of the small intestine varied from a trace to 1·2 mg. After the injection of calcium chloride into the femoral vein the excretion into the intestine was increased little if at all. When doubts regarding the validity of the excretion into the small intestine were thus raised, it was natural that the site of this hypothetical excretion should be transferred to the large intestine, although both Walsh and Ivy and Taylor and Fine had shown that such an excretion was slight. More recently further doubt has been thrown on excretion from the colon by the work of Stewart and Percival, Nicolaysen, and Welch, Wakefield and Adams, who in a human subject with an isolated colon, found in a fourteen-day accumulation of the colonic contents

only 35 mg. of calcium. Wright, Florey, and Jennings, having stimulated a flow of intestinal juice in the colon of cats, found the juice to contain only 2 mg. of calcium per 100 per c.cm.

It is questionable then whether excretion, other than in the digestive juices, takes place to any extent in the intestine. Yet it is from the total (urinary and fæcal) output that the calcium requirement is ultimately deduced. Sherman has used a comparison with protein to justify the standard of calcium requirement that he has laid down. It is not a proper analogy, for there are many varieties of protein and, so far as is known, only one kind of calcium. Moreover, the behaviour and the function of the two substances within the organism are dissimilar. He might have argued with equal justice that, since the end-products of protein katabolism are soluble and probably completely excreted in the urine, it would be logical to assume that the soluble calcium salts which appear in the urine represent the calcium which has been participating in tissue activities and thus represent the real loss which has to be made good.

Sherman, as noted above, has laid down a standard requirement for calcium, but the data from which he derived his figures are difficult to accept. He collected from the literature 97 experiments where an attempt had been made to determine the calcium balance. After he had made certain corrections for the weight of the subjects, he found the mean value of the average daily intake to be 0·45 g., to which value he added a "factor of safety" of 50 per cent., giving the final daily requirement as 0·68 g. In the 97 experiments the level at which equilibrium was attained varied in the individual subjects from 0·27 g. to 0·82 g. a day—i.e., from just about 50 per cent. below the average to almost 100 per cent. above it. To do Sherman justice, he did not originally emphasise his figures as being a final value. He has written recently: "For the purpose of covering individual and accidental fluctuations in actual need an allowance of 0·68 g. per day, which provides a margin of 50 per cent. over the base-line average of 0·45 g., came into very general use: and probably because of the use, it tends to take on more weight of significance than its origin justifies." Later he goes on to say: "For optimal nutrition . . . we must estimate the calcium requirement at not less than 1 g. per day for adult maintenance." In view of the source of his data I think Sherman is more than justified in saying that his findings are given more weight than their origin justifies. Leitch, as the result of a statistical study of many calcium-balance experiments in the literature, has found that positive balances may apparently be attained with an intake as low as 0·15 g. and negative balances with intakes as high as 0·7 g. She concludes that the daily requirement for an adult is reached with an intake of 0·55 g. The allowances she deduced for children are considered by Sherman "uncalled for."

How many of the experiments on which these estimates are based gave a true representation of the calcium balance? One of the great difficulties in carrying out balance experiments on the mineral constituents is the long time that must elapse, many weeks and even in some cases months, according to Berg, before true equilibrium is attained. In any case, Berg does not believe it possible to lay down any specific quantity of a mineral substance as being necessary, for the need is dictated by other factors in feeding. He believes it is much more important to have proper ratios between the various essential minerals. Durig is much of the same opinion. He maintained that "our knowledge is far too limited to allow us to lay down standards relating either to calcium needs or to the means of their satisfaction." The conclusion that the time is not yet ripe for rigid standards seems to be supported by the first report of the Advisory Council on Nutrition of the Commonwealth of Australia, where it is recorded that, if the American standard of 0·68 g. calcium for an adult male (and 1·0 g. for an adult woman and for children) were adopted, only about 3 per cent. of several hundred Australian families investigated would reach the standard. It is not generally held that the Australians are defective in health or physique.

VARIATION IN UTILISATION OF CALCIUM

Further, there is the question of the variation in the utilisation of the calcium in ordinary food. It has always been assumed that the calcium of milk is readily utilised by children, but the recent paper by Kinsman, Outhouse, and Mitchell shows that the mean utilisation value by pre-school children is only some 20 per cent., a very different figure from that given by Ellis and Mitchell of 98 per cent. for rats. It is interesting, in view of the difficulties surrounding the excretion of calcium, to note that there is some evidence that calcium which is released in endogenous metabolism can be reutilised by the organism. Here again output does not give any exact clue to the changes taking place within the living cells. Too often bone is regarded as a mere static skeletal component, whereas it is a relatively active site of metabolism. There is still another practical difficulty. Although a proper amount of calcium may be ingested, there may also be present in the diet some other material, such as oxalic or phytic acid, which will combine with the calcium and render it unabsorbable. It is true, for example, that spinach is relatively rich in iron, but unfortunately it is also rich in oxalic acid, and experiment has definitely shown that if milk and spinach are taken together there is a definite reduction, depending on the relative amounts of calcium and oxalic acid present, in the amount of calcium utilised.

When we turn to the practical aspect of the metabolism of calcium in connexion with rickets and osteomalacia, there are many observations very difficult to explain. For example, Wilson, in her recent study of the diets and health of the inhabitants of a valley in the Punjab, where rickets and osteomalacia are rife, found that the diets were grossly deficient in calcium and vitamin D. This might have been anticipated, but in another area of India, where the environmental conditions and the diet were similar and the food equally deficient, rickets and osteomalacia were almost unknown. Further, she showed that there was no correlation between calcium intake and the incidence of rickets and osteomalacia. Moreover, the children with severe rickets have excellent teeth. Bull, in her recent study of over 1000 Melbourne children under school age, did not find any significant difference in the incidence of caries in well-fed and badly nourished children (using the Emerson standard). She also investigated the relation of caries in children between two and five to the antenatal diets of their mothers. "Of 136 children whose mothers gave a history of deficient antenatal diets 47 per cent. had carious teeth: of 59 whose diets were moderate 34 per cent. had carious teeth and of 126, where the antenatal diet was considered adequate, 46 per cent. had carious teeth." Some of the deficient diets were very bad, but no diet was considered adequate without at least one pint of milk a day, a liberal amount of butter, eggs, green vegetables and fruit, with a sufficient quantity of meat and fish.

There is another assumption in the doctrinaire discussion of diets which is well known to be false—that modern man consumes the same food day in day out all the year round. Obviously, to reduce discussion to manageable proportions, some such assumption must be made; but I suggest that it is physiologically unsound to aim at a constant optimal intake day after day—an intake which probably contains an excess of all the essential proteins, salts, and vitamins. The body was designed with high "factors of safety"; it does not lead a hand-to-mouth existence. Indeed one might say that variability in the supply of food is a more admirable physiological arrangement than constancy of provision.

Before leaving this problem of variation I wish to refer to the importance of appetite. Too often appetite is looked at askance as mere sensual desire, but I am inclined to think that it is unduly belittled. Pavlov's experiments proved, in dogs at least, that appetite was a potent factor in gastric digestion. Appetite is a much more complex sensation than either hunger or thirst; it might indeed be regarded as a fine-gauge "hunger" sense. True, it often does represent merely a desire for the gratification of the palate, or a demand for the food one is accustomed to—the nostalgia for pies as mother made them. But may it not sometimes be evidence of a physiological pica, of the need for the correction of some somatic imbalance? The phenomenon of pica, the consumption of edible earths by certain colonial populations, and the mass movement of wild animals to salt-licks support the contention that somatic needs can determine appetite. This view receives further support from the observations of Mendel and Mitchell on rats and mice and from those of Evvard on the selective appetite of swine for mineral substances. Appetite, then, must be taken into consideration as a dietary guide.

NERVOUS CONTROL OF METABOLISM

There is another aspect of cellular activity in relation to nutrition which has not received the attention it deserves. This is probably due in part to the difficulty of attack. Because we have become so obsessed with the hidden secrets of the metabolic chemical activities in the tissue cells, or perhaps because so many workers in the field of metabolism are chemists and not biologists, it has been forgotten or it is not realised that these metabolic processes may to some extent be under the control of the nervous system. The living organism is not merely a laboratory test-tube in which to carry out a series of complicated physico-chemical reactions. It has long been common knowledge that puncture of the floor of the fourth ventricle is followed by glycosuria. There is, too, some evidence that certain aspects of the water balance of the body are related to the integrity of the tuber cinereum. Grafe has suggested that the midbrain can exercise some form of inhibitory control on protein metabolism, and in the same area there may be some kind of control of the metabolism of fat. There is also experimental evidence that section of the sympathetic nerves interferes with the storage of fat. Further, there seems to be no doubt that there is in the hypothalamic area some kind of centre intimately linked with the control of body temperature, a control which immediately or ultimately requires an adjustment of metabolism.

Turning to a more obvious type of disturbance—atrophy or hypertrophy of muscle—we meet with clear evidence, more particularly in the case of atrophy, of the part played by the nervous system in the control of tissue nutrition. Atrophy results either from simple disuse or from pathological disturbance, such as anterior poliomyelitis. There is also evidence that metabolically two types of atrophy may exist, for atrophy following disuse may take place after deafferentation at the posterior roots, whereas in atrophy associated with a condition like arthritis the afferent paths must be intact. Disuse atrophy might be assumed simply to result from the absence of physiological activity, but Ollerenshaw and Smith have described cases of certain congenital conditions where the muscle was unable to function normally but no atrophy or degeneration took place. Cuthbertson found in normal subjects at rest in bed that within a day or two of the start of the muscle rest there was a rise in the output of nitrogen, sulphur, phosphorus, and calcium in the urine. This loss continued for various periods and then declined. The sulphur: nitrogen ratio suggested that it was muscle tissue which was being broken down, a surmise which was strengthened in later experiments, where it was shown that the potassium output also increased. The same train of events follows when the disuse is the result of an accident, such as a fracture of a leg from direct violence, or, more particularly, of any incapacitating injury to the knee. A difference between the two types of atrophy is that muscular wasting associated with bone and joint disease is much more rapid and extreme than that which follows simple disuse of the limb. That the atrophy is probably due to some unknown trophic disturbance is supported by the fact that the breakdown of nitrogen-containing tissue is not due simply to a lack of food; for, when Cuthbertson increased the food intake even to 5000 calories, with an ample supply of first-class protein, he failed to prevent a negative nitrogen balance at the height of the catabolic phase. On the other hand, in certain control experiments on rats with fractured femurs it was demonstrated that a supplementary ration of cane sugar spared to a considerable extent the loss of body substance.

Whether or not there are nerves with trophic function which are responsible for the physiological condition of normal muscle has led to much debate. I incline to the view that some form of nervous control exists. These nerves act either indirectly through the control of the blood-supply and possibly through the internal secretions or directly on the cell chemistry or possibly by a combination of direct and indirect action. The atrophies which may be found are not necessarily confined to groups of muscles, as for example in anterior poliomyelitis; the extreme emaciation which may occur in certain of the neuroses and psychoses must not be forgotten. Whether anorexia nervosa is or is not a form of Simmonds's disease is not a matter for discussion here. The emaciation is dramatic. Nor must we overlook other curious and interesting conditions such as herpes zoster and "glossy skin" and the curious exacerbations of symptoms which may take place in, for example, duodenal ulcer and mild glycosuria as the result of an emotional state such as fear or anxiety. Finally there are also the astonishing manifestations of hysteria and hypnotic suggestion. I think that we take too much for granted in our simple chemical accounts of the metabolic activities in the living cell.

ENVOI

The mystery can be elaborated in every phase of alimentation and in relation to every constituent reputed to be of value to the organism. For instance, why do the Eskimos develop only the mildest of ketosis in starvation? How do they survive on the minimal intake of carbohydrate? Why is it essential,

as Stefansson found, that if one is to live as the Eskimo does mainly on meat the meat must contain a certain proportion of fat? Lean meat will not suffice. Why does it seem to be essential, as Krogh, Lindhard, and Christensen have shown, that before dextrose can be used to provide energy for muscular action it must first be converted into some other form, probably glycogen? Why is it that in an extreme state of inanition, such as anorexia nervosa, there is rarely any sign of mineral or vitamin deficiency? The problems are endless. We indeed see through a glass darkly; yet every day pronouncements are brazenly made about the adequacy of this and the inadequacy of that diet or the degree of malnutrition which is due to the absence of this or that essential constituent from the diet. Mendel was right when he wrote: "There is no field of practical importance related to human well-being in which there is greater opportunity for dogmatism and quackery, for pseudo-science and unwarranted presumptions and proscriptions, than in the domain of our daily diet."

DILUENTS FOR STORED BLOOD

By Montague Maizels, M.D. Lond., M.R.C.P.
clinical pathologist at university college hospital, london; and
Norman Whittaker, M.B. Camb., M.R.C.P.
medical registrar at the hospital
(*From Emergency Blood-transfusion Centre, Maidstone; Medical Research Council*)

It is not difficult to store blood in good condition for two or three weeks, but towards the end of a month deterioration usually sets in, and the sample rapidly becomes useless. If it were possible to keep blood for two or three months, waste would be eliminated, and it might become unnecessary to localise supplies to the "blood banks." Indeed, it would be possible to distribute to isolated centres and to ships at sea small supplies of blood for use in emergency transfusion. The present paper is mainly concerned with the storage of bloods for long periods.

We have already shown (Maizels and Whittaker 1939) that the tonicity of the standard citrate-saline chiefly used in this country for storing blood is greater than that of fresh erythrocytes. This standard solution contains sodium citrate 1·05 per cent. and sodium chloride 0·85 per cent. On purely experimental grounds it was suggested that the amount of sodium chloride ought to be decreased to 0·43 per cent. We also showed that the addition of dextrin to citrated blood delayed hæmolysis. Sufficient time has elapsed since these observations were made for the effects of tonicity and carbohydrate content to be followed over a period of several months. During this time evidence has been forthcoming that the reaction at which blood is stored is also important. Hitherto our criteria of the destruction of cells have been the amount of spontaneous hæmolysis (H_s), the amount of hæmolysis in saline solutions, and the excess of the colour-index (C.I.) over 1. If the normal colour-index is taken as unity, theoretically H_s should equal $\frac{\text{C.I.} - 1}{\text{C.I.}}$. In this paper we have preferred to give the more comparable value $\frac{\text{C.I.} - 1}{\text{C.I.}}$ rather than the colour-index itself. Table I shows that, when due allowance is made for experimental error, the agreement between H_s and $\frac{\text{C.I.} - 1}{\text{C.I.}}$ is fairly close, the latter expression being usually greater, probably owing to lysis of erythrocytes during their passage through the narrow capillary tube of the hæmatocytometer pipette. Both values are closely parallel to the values of the fragility of cells in saline (Maizels and Whittaker 1940), and the amount of spontaneous hæmolysis is probably an adequate index of destruction of cells. The fact that one blood is less hæmolysed than another must mean that it is in better condition and is more likely to survive after transfusion; but, on the other hand, it is possible that a blood which seems much superior in vitro may survive only slightly longer after transfusion. Tables I–III give data relating to hæmolysis, including mean volume of cells and, in some cases, values for blood-sugar and erythrocyte sodium.

EFFECT OF TONICITY ON SURVIVAL OF CELLS

In general, it may be said that cells stored with isotonic solutions suspend more readily and come away from the sides of the containing vessel more cleanly than when the standard hypertonic solution is used. Apart from this there is little obvious difference during the first month of storage. During the second month spontaneous hæmolysis and high colour-indices are commoner in bloods stored with hypertonic saline; the difference is not striking, but it is definite and consistent, and it may be surmised that the advantages of isotonic storage will be much more evident after transfusion. Cells stored in hypertonic solution become hypertonic, and relative to them fresh normal plasma is hypotonic and hæmolytic. This may be shown in the following way:—

Two samples of the same blood were stored one with isotonic and the other with hypertonic citrate-saline. After two weeks they were centrifuged, and the deposits of cells were mixed with fresh normal plasma derived from heparinised blood. They were then again centrifuged. No hæmoglobin staining of the supernatant fresh plasma was observed in either case, but after six weeks' storage the cells stored in isotonic citrate-saline plasma again showed no further hæmolysis in fresh plasma, whereas the cells kept in hypertonic plasma showed an additional 31 per cent. hæmolysis.

In a second experiment also no hæmolysis was observed after short periods of storage, but after six weeks the isotonic blood was unaffected, whereas just over half of the hypertonic cells were hæmolysed immediately by fresh plasma. This hæmolysis by fresh plasma may be expected to take place not only in the test-tube but also after transfusion. Unless some other special reason is forthcoming, it is probable that isotonic solutions should be used for long storage.

One result of storing erythrocytes is a striking increase in their sodium content; this confirms our previous view (Maizels and Whittaker 1939) that stored cells lose their impermeability to cation. Fresh cells contain about 25 mg. of sodium per 100 c.cm. (Oberst 1935); within a few hours the amount of sodium has nearly doubled; within a week the increase is fivefold, and after six weeks' storage it may be eightfold. When cells are stored in isotonic citrate plasma, the increase in the percentage of sodium is correspondingly less. One thing is clear: the cation content of stored cells is very different from that of fresh erythrocytes, and the striking increase in sodium may be used to solve the vexed question of how long stored blood survives after transfusion. Thus, if a litre of such blood is given to a patient whose hæmoglobin has fallen to 30 per cent., cell sodium will

TABLE I

Expt.	Anticoagulant	Storage (days)	Spontaneous hæmolysis (per cent.)	$\frac{(C.I. - 1)}{C.I.}$	Mean cell volume (μ3)	Cell sodium (mg. per 100 c.cm.)
1	—	0	0·0	− 3	86·0	28
2	Hypertonic	¼	0·0	− 5	78·0	51
3	,,	7	0·0	0	95·5	136
4	,,	7	0·0	− 7	94·0	155
5	,,	13	0·5	6	110·0	139
6	,,	14	3·0	3	100·0	—
7	,,	16	0·5	4	112·0	167
8	Isotonic	16	0·5	− 3	108·0	149
9	,,	16	1·0	0	115·0	147
10	Hypertonic	17	0·5	2	—	162
11	,,	24	4·0	5	110·0	212
12	,,	28	10·0	15	118·0	—
12a	Isotonic	28	8·0	9	109·0	—
13	Hypertonic	28	7·0	6	107·0	—
13a	Isotonic	28	5·0	0	107·0	—
14	Hypertonic	33	19·0	20	107·0	—
14a	Isotonic	33	15·0	22	113·0	—
15	Hypertonic	36	37·0	42	—	—
15a	Isotonic	36	23·0	30	—	—
16	Hypertonic	42	13·0	14	114·0	230
16a	Isotonic	42	11·0	13	121·0	213
17	Hypertonic	46	24·0	12	126·0	240
17a	Isotonic	46	14·5	13	118·0	222

rise from about 25 mg. to 50 mg. per 100 c.cm., and the persistence of this raised amount of sodium after transfusion will be a measure of the survival of the transfused cells. Further, the data may be adapted to show the blood volume of the recipient at the time of transfusion. We are now investigating this point. Cell volume shows fairly wide variations, and little difference is noted in the volume of cells in isotonic or in hypertonic citrate-saline. There is some correlation between mean cell volume and sodium content, the two tending to increase together. The agreement is not close, probably on account of the high experimental error in estimating mean cell volume, especially when partial hæmolysis is present.

Storage affects erythrocytes in several ways: it destroys its normal impermeability to salts, either by a slow chemical disintegration of the cell membrane or by physical changes in the membrane, whose structure may remain more or less intact. In either case diffusion proceeds until the concentrations of salt within and without the membrane are equal. At this stage cell osmotic pressure due to hæmoglobin is unopposed and water continues to flow into the erythrocyte until lysis results. In the process of penetration by salt there are two factors: the difference in salt concentration on the two sides of the membrane—i.e., the concentration gradient—and the permeability coefficient of the membrane. If the cell membrane were freely permeable to salts, increase in external tonicity would have no effect on the time taken for the cell to hæmolyse; for, while the steeper concentration gradient would cause salt to enter the erythrocyte more rapidly, it would be necessary for a much greater absolute amount of salt to enter the cell before the unduly high external concentration of salt were balanced. It is, however, probable that the cell during storage remains relatively though not absolutely impermeable to salts, and that the amount of salt transmitted within a given period of time is fairly constant and not greatly influenced by the concentration gradient. In this event suspension of cells in hypertonic solution will only slightly increase the amount of salts diffusing into the cell, while persistence of a high external concentration of salt will prevent the inflow of water and so tend to check hæmolysis. The data in table I show that hypertonic solutions cause more hæmolysis than isotonic solutions and, in accordance with preceding arguments, suggest that hypertonic solutions injure the cell membrane. Indeed, it is probable that hæmolysis in vitro would be even greater, were it not for the restraining influence of external hypertonicity on swelling of the cell. On the other hand, it must be recalled that a hypertonic anticoagulating solution makes the erythrocyte hypertonic and renders it liable to hæmolysis by fresh normal plasma.

EFFECT OF REACTION ON SURVIVAL OF CELLS

It is well known that cations penetrate erythrocytes with difficulty. The impermeability is greatest at low pH (Mond 1928; Maizels 1935). Cells stored at slightly acid reactions may therefore be expected to admit less sodium and hence to swell and hæmolyse less. This hypothesis was confirmed in the following way: various amounts of N/2 HCl were added to citrate-saline blood. A month later the specimens were examined for pH, spontaneous hæmolysis, and sodium and sugar contents (table II); the pH was estimated approximately with indicator dyes. It will be seen that high acidity causes hæmolysis but, in the presence of a slightly acid reaction, less sodium penetrates the cell and hæmolysis is correspondingly decreased. This is not due to the lower pH inhibiting glycolysis and so favouring preservation of the cells, because sugar contents were similar in all specimens

TABLE II

Expt.	pH	Spontaneous hæmolysis (per cent.)	Sugar	Sodium
			mg. per 100 c.cm.	
1	7·25	11·0	21	185
	6·7	4·5	28	149
	6·5	4·5	—	—
2	7·2	7·5	22	207
	6·5	5·5	—	144
	6·0	21	—	—
3	7·8	3·0	10	180
	6·5	0	8	82
4	7·4	3·0	11	183
	6·2	0	15	96

examined. The facts may best be explained on the view that high pH takes the cell membrane further away from the isoelectric point of the stroma protein (about pH 5 according to Jörpes, 1932) and thus favours penetration of cations. If it should ultimately prove desirable to store blood under slightly acid conditions, it might become necessary to neutralise before transfusion by adding the equivalent amount of alkali to the supernatant plasma of a stored blood and then mixing thoroughly and rapidly.

EFFECT OF CARBOHYDRATE ON SURVIVAL OF CELLS

The statement that dextrin aids the preservation of stored blood is confirmed in a striking manner by the

TABLE III

Expt.	Solution	Storage (days)	H_s %	(C.I. − 1) / C.I. %	M.C.V. (μ3)	Cell Na	Blood glucose*
						mg. per 100 c.cm.	
A	H	28	10·0	15	118	—	42
	I	,,	8·0	9	109	—	29
	I + D (9%)	,,	0·0	− 3	103	—	331
	I + G (1%)	,,	0·5	—	105	—	55
B	H	28	7·0	6	107	—	16
	I	,,	5·0	0	107	—	29
	I + D (9%)	,,	0·5	− 5	95	—	842
	I + G (%)	,,	0·5	—	—	—	29
C	H	33	19·0	20	107	—	24
	I	,,	15·0	22	113	—	20
	I + D (6%)	,,	1·0	1	108	—	253
	I + C (2%)	,,	6·5	—	—	—	29
	I + G (0·3%)	,,	6·5	—	—	—	73
D	H	34	19·0	—	—	238	31
	H + D (9%)	,,	2·5	—	—	217	384
	H + G (3%)	,,	3·0	—	—	198	552
	H + C (3%)	,,	10·0	—	—	—	—
E	H	34	19·0	—	—	216	27
	H + D (9%)	,,	1·0	—	—	204	384
	H + G (3%)	,,	1·0	—	—	198	580
	H + C (3%)	,,	10·0	—	—	—	—
F	H	37	13·0	21	—	—	27
	I	,,	11·0	18	—	—	24
	I + D (6%)	,,	1·0	1	—	—	354
	I + G (0·3%)	,,	3·0	—	—	—	59
	I + C (1%)	,,	5·5	—	—	—	23
G	H	42	13·0	14	114	230	30
	I	,,	11·0	13	121	213	30
	I + D (9%)	,,	2·0	− 3	94	182	880
	I + G (1%)	,,	3·0	5	—	—	182
H	H	46	24·0	12	126	240	12
	I	,,	14·5	13	118	222	16
	I + D (9%)	,,	1·5	− 7	98	204	432
	I + G (1%)	,,	2·5	—	—	—	136
I	H	84	29·0	—	—	—	10
	H + D (9%)	,,	5·5	—	—	—	183
J	H	84	26·0	—	—	—	8
	H + D (9%)	,,	2·0	—	—	—	190
K	H	100	30·0	—	—	—	—
	H + D (6%)	,,	8·0	—	—	—	—

H = Sodium chloride 0·85 per cent. Sodium citrate 1·05 per cent.
I = Sodium Chloride 0·43 per cent., Sodium citrate 1·05 per cent.
D = dextrin G = glucose C = cane sugar
H_s = spontaneous hæmolysis C.I. = colour-index
M.C.V. = mean cell volume
* = reducing substances reckoned as glucose.

data in table III. Swelling of the cells is reduced by 10–20 per cent., and the final content of sodium is also about 20 per cent. less. If allowance is made for the swelling of cells stored in simple salt solutions without dextrin, it may be shown that in the absence of dextrin about 35 per cent. more sodium penetrates the erythrocyte membrane than in its presence. Inulin has a similar effect, but cane sugar is much less effective. Glucose, on the other hand, is most efficient, for if the anticoagulant solution contains 0·3 per cent. of glucose, corresponding to an overall increase of only 0·1 per cent. in the citrate-saline-blood mixture, hæmolysis is reduced by more than half. The period of storage was six weeks, and at the end of this period the amount of reducing substance remaining, estimated as glucose, was only about 60 mg. per 100 c.cm. In solutions containing no added carbohydrate reducing substance present after six weeks' storage was less than 30 mg. per 100 c.cm. and was often too small to be measured accurately. When 1 per cent. of glucose is added to citrate-saline, survival of cells is further improved, hæmolysis being less than a quarter of that observed in the absence of glucose, though it is about twice as great as that noted in the presence of dextrin. After six weeks of such storage reducing substances in the stored blood have declined from about 400 mg. per 100 c.cm. (including 100 mg. originally present in the blood before dilution) to roughly 100 mg. per 100 c.cm. If the glucose content is 3 per cent. (1 per cent. overall), reducing substance at the end of five weeks' storage is about 500 mg. per 100 c.cm., the merest trace of hæmolysis is present, and preservation is as good as with dextrin. When dextrin is added, preservation is, as we have seen, excellent after seven weeks' storage, and even after a hundred days the cells are still in good condition, after which period reducing substances in the blood are a little under 200 mg. per 100 c.cm., while besides these there is probably a reserve of unhydrolysed polysaccharide. It therefore seems most probable that, where preservation of blood for periods up to two months is desired, glucose may be added to blood, a procedure recommended also by Gwynn and Alsever (1939); but, when attempts are made to keep blood for three months or more, dextrin should be preferred. Our present practice is to sterilise 270 g. of glucose in a dry MacCartney bottle at 105° C. in a hot-air oven. After twelve hours the bottle is partially cooled and hot sterile water is added to the 540 c.cm. mark. The bottle is closed with a rubber washer and a perforated screw cap and placed in an incubator at 37° C. until the sugar dissolves. This procedure avoids caramelisation of the sugar. With a 50 c.cm. syringe and needle 10 c.cm. of the glucose solution is added to each of ten bottles containing citrate-saline blood, the needle being entered through the hole in the screw cap. In this way the sugar content of the blood is increased by 1·0 per cent.

Preservation by carbohydrate may be brought about in several ways: (1) sugar may act as a source of nutrition and so help to maintain the natural impermeability of the cell membrane; (2) it may allow the cell membrane to stretch to a greater extent, so that the cell can accommodate more salt and water than it can in the absence of carbohydrate; and (3) carbohydrate may assist storage by altering the reaction of the blood.

(1) *Improved nutrition of the cell membrane.*—That some such process must take place is shown by the smaller volume and lower sodium content of cells stored with carbohydrate.

(2) *Increased extensibility of the cell membrane.*—Carbohydrate is associated with good preservation and absence of hæmolysis, even when swelling of the cell is comparatively great. In a previous paper (Maizels and Whittaker 1940) it was suggested that glucose became incorporated in the surface of the cell and so increased the area of the surface. The membrane of the cell is only two or three molecules thick (Danielli 1935), and an adsorption of this nature is possible. Evidence for this view is the fact that erythrocytes placed in increasing dilutions of sodium-chloride solution swell and eventually hæmolyse. The maximal swelling obtainable in the absence of hæmolysis is, in the case of salt solution, 64 per cent.; if glucose 1 per cent. is added to the salt, 84 per cent. swelling can be obtained before hæmolysis appears. With lævulose 1 per cent. it is 81 per cent.; with cane sugar, lactose, and maltose 1 per cent. 73 per cent. of swelling can be attained, and with dextrin 1 per cent. subhæmolytic swelling is only 70 per cent., and even this small increase over the maximal swelling obtainable in saline may be due to the glucose content (6 per cent.) of the preparation of dextrin. In accordance with these observations, it is found that glucose is most efficient in preventing the deterioration of stored blood; cane sugar is much less effective, and dextrin, which probably acts by liberating glucose, is as

effective as glucose and is perhaps even to be preferred for prolonged storage.

(3) *Reaction at which blood is stored.*—Blood stored with simple citrate-saline for several weeks has a pH between 7·8 and 7·4—sometimes as low as pH 7·2. In the presence of glucose or of dextrin the pH is between 0·2 and 0·6 less. It has already been shown that slight acidity favours preservation of the cells and decreases hæmolysis considerably; but the effect of adding carbohydrate, which reduces hæmolysis to about a tenth of that found in its absence, is so much greater that pH probably plays a minor part when carbohydrates are used to preserve blood.

SUMMARY

(1) The cells of blood stored with the standard citrate-saline solution (sodium chloride 0·85 per cent., sodium citrate 1·05 per cent.), which is in fact hypertonic, are hypertonic, whereas cells stored with a truly isotonic solution (sodium chloride 0·43 per cent., sodium citrate 1·05 per cent.) are isotonic After a month's storage the hypertonic cells show rather more hæmolysis. If the unhæmolysed cells of each system are then mixed with fresh normal plasma, the hypertonic erythrocytes show a further 50 per cent. hæmolysis, and the isotonic cells show no lysis at all. Blood-cells stored with a truly isotonic anticoagulant solution are therefore much more likely to survive after transfusion. If storage is prolonged, sodium salts flow into the cells, which swell and finally hæmolyse.

(2) If acid is added to a saline-citrate-blood mixture so as to decrease the pH to about 6·6, hæmolysis is reduced by about half, probably owing to decreased penetration of cation at low pH.

(3) If carbohydrate is added to stored blood, sodium penetration and cell swelling are decreased, and at six weeks hæmolysis is about a tenth of that observed in simple salt solutions.

(4) A suitable anticoagulant diluent for blood is sodium chloride 0·43 per cent., sodium citrate 1·05 per cent. It is, however, probably desirable to add glucose or dextrin in a final concentration of 1·0 and 3 per cent. respectively to improve preservation. If this is done, the system becomes slightly more acid, and to counteract cell swelling due to acidity it may be desirable to increase the content of sodium chloride in the solution to 0·5 per cent.

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THE voice has its scientific aspect, although both singers and physiologists are apt to ignore it. Attention has been drawn to this omission recently by two very different books. In "The Physiological Basis of the Art of Singing" (H. K. Lewis and Co. 1939. Pp. 139. 10*s*. 6*d*.) Mr. Hayden Hemery, L.R.A.M., has approached the subject from the point of view of the teacher of singing, and he mixes up science with precept and philosophy. The best part of the scientific treatment is the clear simplified anatomical illustrations. Mr. Robert Curry, Ph.D., has come to be interested in the human voice after a study of psychology and experimental phonetics. In his "Mechanism of the Human Voice" (J. and A. Churchill. 1940. Pp. 205. 10*s*. 6*d*.) he has produced a valuable and concise book which summarises recent researches. It fills a unique place in scientific literature, and with its good bibliography is valuable both for information and reference.

TUMOUR CELLS IN STERNAL BONE-MARROW

BY LEIV KREYBERG, M.D.
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF OSLO
AND
ERIK POPPE, M.D.
(*From the Norwegian Radium Hospital*)

SINCE Arinkin (1929) published his important paper, sternal puncture has been commonly used in diagnosis, especially in diseases of blood and bone-marrow. It has also been described as of value in the diagnosis of malignant tumours. Rohr and Hegglin (1936) described smears of sternal bone-marrow in 74 cases of malignant tumours; in 12 of these cases there were extensive metastases in bone, 10 of them showing tumour cells in the smears. Rohr and Hegglin found two kinds of cells, derived from large-celled and small-celled tumours, and they concluded that it was not possible to diagnose from smear preparations the type of the primary tumour. Their large cells were characterised by a considerable anisocytosis, a large nucleolus, and an increased ratio of the nucleolus/nucleus size. They claimed that they could diagnose large-celled tumours from a single cell in a smear; but groups of cells in a smear were necessary for a reliable diagnosis of small-celled tumours.

We have examined the sternal bone-marrow in 100 patients with malignant tumours of different types and in different stages. We have made parallel series of smears and of sections of embedded preparations. The material for the sections was collected in the following manner :—

Sternal bone-marrow 2–3 c.cm. is aspirated with a strong syringe and placed in a petri dish. By gentle manipulation of the dish and the use of a glass rod or a cover glass the particles of marrow are brought together to form a solid mass, whose size may vary from that of a hemp seed to that of a small bean. This lump is fixed in Zenker's fluid, embedded in paraffin, cut in sections, and stained. Our technique differs from that of Rothe Meyer (1936) by the use of larger quantities of bone-marrow.

In 8 out of the 100 cases tumour cells were found in the sternal bone-marrow, and in all these 8 cases the patients showed clinically and radiologically metastases in bone, lymphatic glands or elsewhere. The main findings were as follows.

CASE 1.—Female, aged 44. Breast cancer in 1932. In January and April, 1939, metastases to spine, pelvis, and skull. Sternal marrow sections are shown in figs. 1*a* and *b*.

CASE 2.—Female, aged 50. Breast cancer in 1933. In April, 1939, metastases to sacrum, sternum, and lung. Sternal marrow section shown in fig. 2. No definite diagnosis from the smears possible.

CASE 3.—Female, aged 69. Breast cancer in 1938. January, 1939, metastases to spine and pelvis. Sternal marrow section shown in fig. 3. No definite diagnosis from the smears possible.

CASE 4.—Male, aged 63. Prostatic carcinoma with metastases to spine, pelvis, ribs, and sternum. Sternal marrow sections shown in figs. 4*a* and *b*.

CASE 5.—Male, aged 65. Prostatic carcinoma with metastases to sacrum and pelvis. Sternal marrow section shown in fig. 5. No definite diagnosis from the smears possible.

CASE 6.—Male, aged 59. Prostatic carcinoma with metastases to pelvis, spine, and ribs. Sternal marrow sections showed an alveolar carcinoma, and the smears gave pictures similar to those shown in figs. 1*b* and 4*b*.

Figures showing sections of sternal marrow fixed in Zenker's fluid

(*a*)

(*b*)

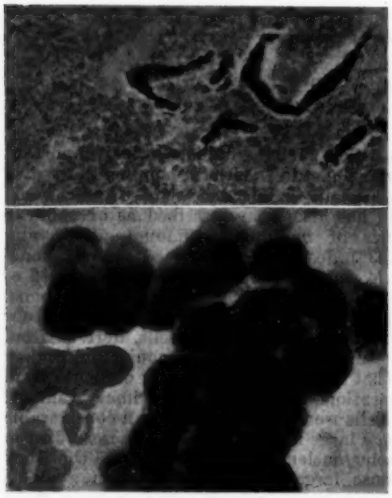

FIG. 1—Case 1 : *a* × 200 ; *b* × 1000.

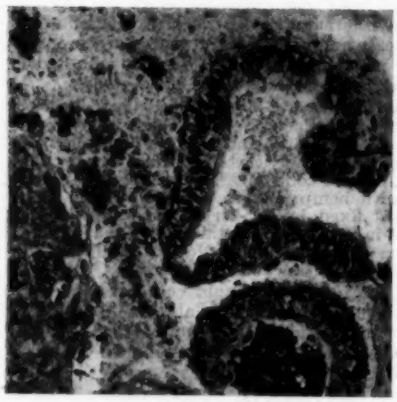

FIG. 2—Case 2 (× 200).

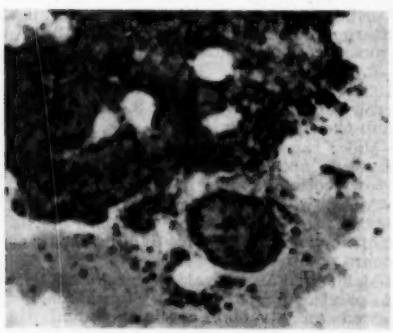

FIG. 3—Case 3 (× 200).

CASE 7.—Female, aged 36. Gastric carcinoma with lymph nodes involved in the supraclavicular fossa. Sternal marrow section shown in fig. 6. No definite diagnosis from the smears possible.

CASE 8.—Male, aged 61. Myeloma. Sections and smears from the sternal marrow permitted a definite diagnosis, many plasmocytes being present.

Since a positive diagnosis of a tumour, based on the appearance of the sternal bone-marrow, was obtained only in cases with widespread metastases, the practical importance and theoretical significance of this diagnostic procedure are limited. In our hands the sections have given a decidedly more reliable method of diagnosis than smears. In the sections the usual histology of the tumour cells and the tissue architecture are to a great extent preserved. The sections therefore enable the pathologist to diagnose a malignant tumour, not merely in vague terms, such as "small-celled" or "large-celled" tumour, but also more specifically, and sometimes they also provide a clue to the origin of the tumour cells. Our findings therefore entirely agree with those obtained by Schlesinger (1939) from examination of thoracic and abdominal fluids.

SUMMARY

Parallel series of smears and of sections of sternal bone-marrow after sternal puncture in 100 patients with

(*a*)

(*b*)

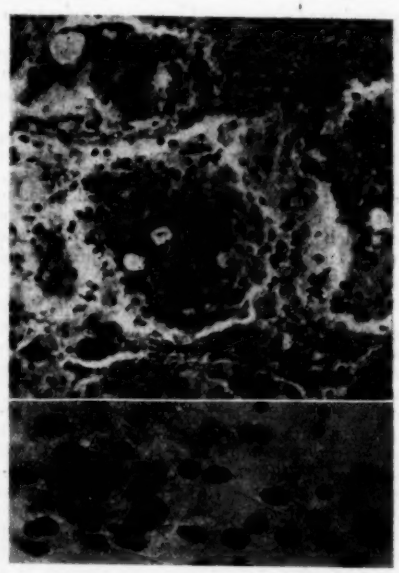

FIG. 4—Case 4 : *a* × 200 ; *b* × 400.

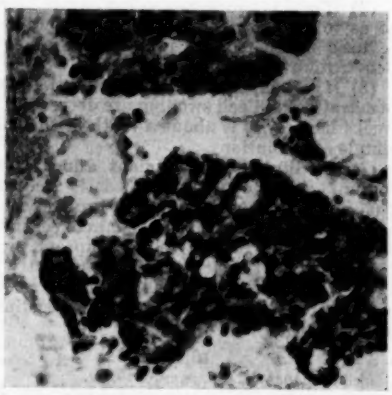

FIG. 5—Case 5 (× 250).

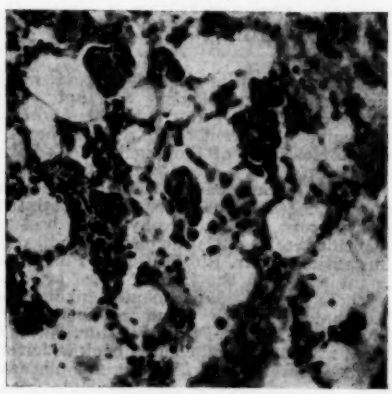

FIG. 6—Case 6 (× 200).

malignant tumours have been examined for the presence of tumour cells. In 8 cases tumour cells were found, and in each of them the disease was in a late stage, with remote metastases. The sections gave a more reliable method of diagnosis than smears. The sections may sometimes give a clue to the site of the primary tumour.

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CAUSE OF BREECH PRESENTATION

BY C. KEITH VARTAN, F.R.C.S., M.R.C.O.G.

ASSISTANT OBSTETRIC SURGEON AT THE MEMORIAL HOSPITAL, WOOLWICH

TEXTBOOKS on obstetrics give the causes of breech presentation as follows:—

Abnormal shaped uterus, contracted pelvis, tumours, low insertion of the placenta, polyhydramnion, multiparity, hydrocephalon, tumours of the fœtal head and neck, prematurity, twins (De Lee, Principles and Practice of Obstetrics, 1938).

Hydrocephalus, hydramnios, premature fœtus, placenta prævia, pelvic contraction, and in many cases none of these conditions is present (Eden and Holland, Text Book of Midwifery, 1938).

(*a*) Prematurity. (*b*) Conditions interfering with the engagement of the head in the pelvis such as contracted pelvis, or disproportion, placenta prævia, pelvic tumour &c., and in many cases no cause can be found (F. J. Browne, Antenatal and Postnatal Care, 1939).

Contracted pelvis, pelvic tumours, obliquity of the uterus, dead or premature fœtus, multiple pregnancy, anencephaly, hydrocephaly, placenta, prævia, hydramnios (Queen Charlotte's Text Book of Midwifery, 1939).

The cause is not always easy to determine and in some cases a satisfactory answer cannot be given . . . (Ten Teachers' Midwifery, 1938).

There is a similarity about these selected passages, and the notes which I took as a student are almost identical. What struck me then and still impresses me concerning the ætiology of breech presentation is that most of these factors which are reputed to be causes very seldom occur. I conclude therefore that either the "cause" is so rare as to be almost a chance coincidence, or that the cause in almost every case is unknown. In an attempt to change this unsatisfactory state of affairs I have made this analysis of 969 cases of breech delivery.

SPONTANEOUS VERSION

That the fœtus can and often does undergo spontaneous version is agreed by obstetricians, and it is a matter of common clinical experience that breech presentations found in the antenatal clinics become progressively less common as term approaches. The cause of this spontaneous cephalic version is still a matter for speculation, but it does not influence the matter in hand, for it is not denied that it takes place. It is also known that the tendency increases with the approach of term. The reason why the breech persists till term is not to be sought in the factors which prevent the head engaging. These cause the oblique lie. The underlying factors must be those which prevent spontaneous version from taking place. It cannot be denied that the presence in the uterus of one or more other fœtuses must hamper the movements which each fœtus is wont to undergo. Multiple pregnancy must therefore be an important factor. Because breech presentation is commoner before term than at term, it follows that premature labour must increase the incidence of breech delivery.

EXTENDED LEGS

Thus far we are all in agreement, and for further information about the factors which militate against the successful performance of external version, I again refer to the textbooks:—

The condition requiring the interference will usually determine the outlook (De Lee).

The operation is more difficult if the legs are extended (Eden and Holland).

Extended legs seem to splint the body and prevent flexion of the spine (Browne).

The legs of the fœtus may be extended and so act as a splint preventing the flexion which is necessary to perform version (Queen Charlotte's).

With every help, version may be impossible if the legs are extended (Ten Teachers).

All are therefore agreed that it is the extended attitude which is the greatest obstacle to the obstetrician; but no-one has suggested till now that this same extended attitude might prevent the fœtus from accomplishing this manœuvre. Table I shows the frequency of the conditions which I have so far mentioned in these 969 breech deliveries. In many

TABLE I—INCIDENCE OF VARIOUS CONDITIONS IN BREECH PRESENTATION

Condition	Queen Charlotte's				Guy's			Princess Mary			City of London			St. Bartholomew's		Total and per cent.
	1935	1936	1937	1938	1935	1936	1937	1937	1935	1936	1929	1934	1937	1936	1937	
Extended legs	60	47	30	24	6	16	14	30	37	30	9	9	28	8	14	362 (37·3)
Multiple pregnancy	30	19	22	22	8	13	13	17	18	24	15	12	12	3	1	229 (23·6)
Prematurity	10	8	7	4	3	2	7	9	7	13	4	6	3	4	2	89 (9·1)
Placenta prævia	1	4	2	2	—	—	2	6	2	7	1	3	—	1	0	31 (3·2)
Disproportion	—	1	—	1	—	3	2	2	—	2	—	2	—	—	—	13 (1·3)
Anencephaly	—	—	1	2	—	1	2	2	—	1	—	—	—	2	—	11 (1·1)
Hydrocephalus	—	—	3	—	—	—	—	3	1	2	—	—	—	—	—	9 (0·9)
Fibroids (? pelvic)	—	—	—	—	—	1	—	—	—	—	—	—	1	—	—	2 (0·2)
Exomphalos	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	1 (0·1)
No abnormality recorded	8	11	9	10	12	5	12	37	25	33	17	15	15	6	7	222 (22·9)
Total	109	90	74	65	29	41	52	107	90	112	46	47	59	24	24	969

TABLE II—ASSOCIATION OF PLACENTA PRÆVIA (PL. PR.) AND OF DISPROPORTION WITH BREECH PRESENTATION

Hospital and year	Total no of pl. pr.	Pl. pr. and breech	Total no. of dispropn.	Disprpn. and breech
Q.C.H. (1935)	34	1	68	—
,, (1936)	33	4	72	1
,, (1937)	25	2	65	—
,, (1938)	26	2	96	1
Guy's (1935)	4	—	40	—
,, (1936)	9	—	40	3
,, (1937)	14	2	55	2
Pr. Mary's (1935) ..	56	2	157	—
,, (1936) ..	59	7	132	2
,, (1937) ..	67	6	143	2
City of Lond. (1929) ..	15	1	35	—
,, (1934) ..	19	3	36	—
,, (1937) ..	22	—	30	—
Bart's (1936)	3	1	8	—
,, (1937)	3	—	9	—
Total	387	31 (8%)	986	11 (1%)

of these cases two or more anomalies have been present together. In such cases the extended attitude has been omitted in favour of the other condition. Cases of 35 weeks and under have been regarded as premature, because the weights of the babies are not given in the breech statistics. From table I it is possible to see at a glance how frequently extension of the legs, multiple pregnancy, and prematurity occur, and how infrequently do the other conditions. The extended attitude is by far the commonest factor; next comes multiple pregnancy; and then prematurity in small but sufficient numbers to be significant. The other conditions taken together do not amount to 7 per cent. Placenta prævia and disproportion form a very small percentage.

PLACENTA PRÆVIA AND DISPROPORTION

Table II gives the total numbers of cases of placenta prævia and of disproportion, and the number of occasions on which these conditions were associated with breech presentation. Unfortunately it has not been possible to do the same with the cases of prematurity, because the standard of maturity varies in the reports and from the standard which I of necessity adopted. Only 8 per cent. of placenta prævias and 1 per cent. of cases of disproportion are associated with breech presentation.

CONCLUSIONS

(1) We have been wrong in teaching that the cause of the breech presentation at term is a pelvic anomaly which prevents the head from entering. Such conditions cause the oblique lie.

(2) The cause of the breech presentation persisting till term is the failure of the fœtus to undergo spontaneous cephalic version.

(3) The fœtus is prevented from undergoing version by its extended attitude in 37·3 per cent. of cases by the presence of another fœtus in the uterus in 23·6 per cent. of cases and by prematurity in 9 per cent.

(4) In 22·9 per cent. of cases no cause is recorded.

(5) The percentage of cases in which placenta prævia is associated is so small as to make it doubtful if this can be called an ætiological factor.

(6) For the same reason contracted pelvis cannot be regarded as an ætiological factor.

(7) Pelvic tumours, abnormally shaped uterus, hydrocephalus, hydramnios, and anencephaly are so rare as to be of little significance.

These figures have been taken from the annual maternity reports of the City of London, Guy's, Princess Mary's (Newcastle-on-Tyne), Queen Charlotte's, and St. Bartholomew's hospitals. The choice was in the first place a random one; those to hand were examined first and all those which contained sufficient detail were used.

I gratefully acknowledge the value that the work of the registrars, Messrs. J. B. Blaikley, S. G. Clayton, R. L. Dodds, B. Gilbert, H. A. Hamilton, P. Playfair, and F. Stabler, has been to me, and I wish also to thank the secretaries of these hospitals for sending me their reports.

PFEIFFER BACILLUS MENINGITIS

SUCCESSFULLY TREATED WITH M. & B. 693

COMPLICATED BY GRANULOPENIA

BY J. SAKULA, M.D. Lond., M.R.C.P., D.C.H.

ASSISTANT RESIDENT MEDICAL OFFICER AT THE CENTRAL MIDDLESEX COUNTY HOSPITAL, WILLESDEN

THE meningitis caused by Pfeiffer's bacillus, rather misleadingly called influenzal meningitis, has always been accompanied by a high case-mortality; therefore complete recovery is of interest. Roche and Caughey [1] have reported two cases successfully treated with M. & B. 693 and have concluded that the good results were pre-eminently due to this drug. In the following case similar treatment had a satisfactory result, in spite of the development of granulopenia.

CASE-RECORD

A girl, aged 2½ years, the third child of healthy parents, none of whom had recently had any colds or influenza, was admitted to the Central Middlesex County Hospital on Dec. 8, 1939. She had had

BLOOD-COUNTS

Date	R.B.C. (millions) per c.mm.	Hb. %	W.B.C. per c.mm.	Granulocytes per c.mm.	Neutrophils %	Eosinophils %	Basophils %	Lymphocytes %	Monocytes %
Dec. 12	5.92	90	25,100	15,311	60	..	1	36	3
20	3.38	63	23,000	18,400	79	1	..	18	2
28	3.95	71	3000	390	13	..	..	84	3
29*	..	63	2100	105	5	..	..	94	1
30	3.86	67	2100	147	7	..	..	87	6
31	..	66	4450	133	3	..	..	94	3
Jan. 1	..	..	5450	272	5	..	..	92	3
3	4.59	70	7750	852	11	..	..	85	4
5	..	69	8350	1420	17	..	..	80	3
6†	..	..	8300	1660	20	..	..	79	1
9	..	..	9000	3060	34	..	..	64	2
12	..	..	13,500	5535	40	..	1	55	4
22	4.60	90	15,500	8990	53	4	1	40	2

* Pentnucleotide started. † Pentnucleotide stopped.

1. Roche, E. H. and Caughey, J. E. *Lancet*, 1939, **2**, 635.

measles and chickenpox during her first year, and apart from a fall a week before admission, when she hurt the back of her head, which upset her for about twenty-four hours, she appeared to be quite well till the day before admission. She then became listless, looked ill, and complained of severe pain in the back of her neck and indefinite pains in the head and abdomen. There was no cough and no sore-throat.

On admission the temperature was 103° F., pulse-rate 128, and respiration-rate 48. She was irritable and resented interference ; she had no head retraction but had definite neck rigidity with a positive Kernig's sign. The ocular fundi and ear drums were normal, and apart from a general redness of the throat and herpes of the upper lip no gross abnormal signs were detected. Meningitis was diagnosed, and lumbar puncture produced turbid cerebrospinal fluid not obviously under increased pressure. The fluid contained 440 cells per c.mm., almost entirely polymorphs, and many gram-negative pleomorphic bacilli in the stained film of the centrifuged deposit, which on culture proved to be the *Hæmophilus influenzæ*.

Treatment with M. & B. 693 was started on the second day of the illness, soon after admission, 2 g. being given during the first day, and the dose being increased to 2·5 g. a day on the next day, when the exact nature of the meningitis was discovered. For three days the child's condition showed little change, but the herpes became more extensive, and she

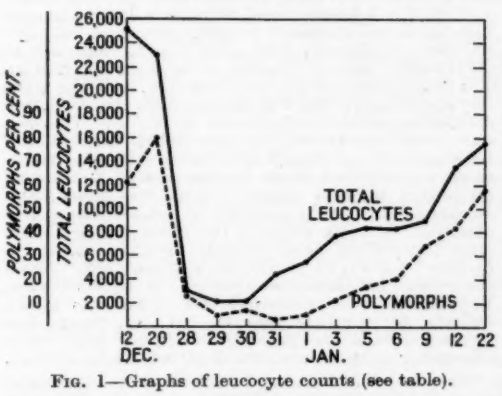

FIG. 1—Graphs of leucocyte counts (see table).

became more irritable and developed stomatitis. On Dec. 13 (the fifth day after admission) she began to improve clinically. Lumbar puncture now showed the cerebrospinal fluid to be almost clear, with the cell-count still raised, but no organisms in the stained film of the deposit, and the culture sterile. At that time the blood-count showed a leucocytosis of 25,100 per c.mm., of which 60 per cent. were neutrophils. (For blood-counts see the accompanying table and fig. 1.)

On the eighth day, when 17 g. of M. & B. 693 had been given, administration of the drug was stopped because the child had developed a generalised toxic rubella type of rash all over the trunk and limbs but not on the face. By the next day (Dec. 16) the rash had almost completely disappeared and the child's general condition appeared satisfactory, except that the herpes showed no sign of clearing. There was no neck rigidity, but lumbar puncture showed the cerebrospinal fluid to contain a few gram-negative bacilli, and culture produced a scanty growth of *H. influenzæ*.

On the 17th the temperature and pulse-rate remained normal, but the child was listless again, and on the 18th she became more drowsy and irritable. During the afternoon the pulse-rate and temperature rose rapidly, and a further lumbar puncture was performed, the fluid being more turbid and under increased pressure. The cell-count was increased to 730 per c.mm. (80 per cent. being polymorphs) and culture again gave a free growth of *H. influenzæ*. In

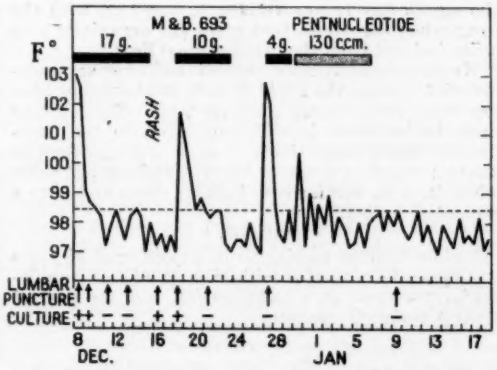

FIG. 2—Chart in a case of Pfeiffer bacillus meningitis treated with M. & B. 693 and complicated by granulopenia.

view of this relapse, and in spite of the toxic rash, it was decided to resume the administration of M. & B. 693, which was now given in doses of 2 g. a day and continued for five days. A blood-count on the 20th still showed a leucocytosis of 23,000 per c.mm., with 79 per cent. neutrophils.

On the 25th the child seemed quite well, the temperature and pulse-rate were settled, and the herpes was now healing well, but on the 27th the temperature and pulse-rate rose, and she became drowsy again, complained of headache, and resented interference. Lumbar puncture was performed, but the fluid appeared clear and not under increased pressure and subsequently proved to be sterile. A further relapse was feared, and it was thought advisable to give her more M. & B. 693, keeping a close watch on the blood-count. On the 28th, however, the leucocyte-count was only 3000 per c.mm., with 13 per cent. neutrophils. The M. & B. 693 was therefore immediately stopped (a further 4 g. having been given) and administration of Pentnucleotide started, at first 10 c.cm. intramuscularly twice a day, but later only once a day.

On the 29th the child seemed quite well. The pulse-rate and temperature had returned to normal, the throat was clear, there was no enlargement of the lymphatic glands, and the spleen was not palpable. The leucocyte-count had, however, fallen to 2100 per c.mm., with only 5 per cent. of neutrophils ; the actual number of neutrophils was 105 per c.mm.

From that day onwards the blood-counts slowly improved, and the child had no further symptoms. The pentnucleotide was continued for nine days, and the blood-count on Jan. 23 showed 15,500 leucocytes per c.mm., of which 58 per cent. were granulocytes. The cerebrospinal fluid on Jan. 9th contained only 14 cells per c.mm., 12 of which were lymphocytes, and the fluid was sterile on culture. On the 25th, seven weeks after admission, the child was transferred to a convalescent home, walking well, free from all symptoms, and weighing 32 lb., having gained 3 lb. since admission.

COMMENTS

The good result in this case must be attributed to the use of M. & B. 693, especially in view of the relapse that took place when the drug was first stopped, and the further dramatic improvement when it was started again (fig. 2). The repeated lumbar punctures were performed for diagnosis only, a few c.cm. being taken off each time. Blood-transfusion, of which the possible benefit in these cases has never been convincing, was not tried. Large doses of M. & B. 693 seemed necessary (a total of 31 g.) and, though carrying the danger of toxic symptoms, were justified in view of the hitherto grave prognosis in this condition. Even after the appearance of the rash on

the eighth day it was decided to carry on with the drug, when the relapse took place and organisms were again isolated from the cerebrospinal fluid.

Numerous cases of granulopenia and even agranulocytosis following the use of M. & B. 693 have now been reported, many cases proving fatal. This danger must be increased in children, in whom the bone-marrow seems more liable to toxic damage than in adults; therefore frequent blood-counts are advisable when M. & B. 693 is given in large doses and over a prolonged period.

SUMMARY

Pfeiffer bacillus meningitis in a child aged 2½ years was successfully treated with M. & B. 693. Granulopenia developed as a complication, but the patient made a complete recovery.

PICROTOXIN IN THE TREATMENT OF COLLAPSE DUE TO BARBITURATES

BY S. W. GILLMAN, M.R.C.S., D.P.M.

SENIOR ASSISTANT MEDICAL OFFICER AT THE WARWICKSHIRE AND COVENTRY MENTAL HOSPITAL, HATTON

THE usefulness of prolonged narcosis in psychiatry has not been diminished by the introduction of shock therapy, and, if the experiences of Mira (1939) in Barcelona are ever repeated here, prolonged narcosis may become the main treatment of acute mental disturbances arising from air-raids. Barbiturates easily take pride of place among the drugs used to produce prolonged sleep, and it is our experience at Hatton that best results are obtained with deep narcosis; this is one reason why dangers and complications arise from time to time, and emergencies have previously been described as arising with Somnifaine (Parfitt 1936) and with a mixture of Medinal and Luminal (Gillman and Wilson 1938). In the main, barbiturates are either rapidly oxidised in the tissues or slowly excreted by the kidneys, but the safer rapidly oxidised barbiturates are not so suitable as the longer-acting drugs for this therapy. I have tried Hebaral sodium in four cases, but it is so quickly broken down by the tissues that the narcosis is jerky, the patient becoming rapidly conscious at intervals, while so much is used to combat this that drenching perspiration and vomiting are common. The smoothness of a narcosis largely depends on the accumulation of slowly excreted drugs, and this is a second reason why undesirable complications occasionally develop.

In a hundred cases treated by medinal-luminal narcosis I have met with four cases of dangerous collapse. Picrotoxin, which increases respiration and the consumption of oxygen (Cohen and Kohn 1937) and is claimed to be superior to other drugs, such as Cardiazol (Krantz et al. 1937), was used in these four cases, as recommended by Bigg et al. (1937), and also in a severe case of medinal poisoning.

CASE-RECORDS

In medinal-luminal narcosis, a mixture is used which is made up in drachm doses, each containing barbitone soluble gr. 5 and phenobarbitone soluble gr. 1. In the first four of the following cases this mixture was administered.

CASE 1.—A female, aged 17, had alternate bouts of mild excitement and depression and had attempted suicide many times. She was in good bodily health. She collapsed on the fourth day of treatment, after having received a total dose of 20 fl. drachms of the mixture, equivalent to medinal gr. 100 and luminal gr. 20. She was unconscious and grey, with stertor and pulmonary congestion, and her corneal and light reflexes were absent. Routine treatment used in this hospital, which consists of a stomach wash-out, hot strong coffee given through a stomach-tube, hot coffee per rectum after an enema, lumbar puncture, warmth and raising the foot of the bed, and Coramine and strychnine given intravenously and intramuscularly, was unsuccessful, the patient's condition remaining unchanged.

Picrotoxin (10 c.cm. of a 1 in 1000 solution) was then given intravenously, and immediately the corneal reflexes and movements of arms and legs returned. Another 10 c.cm. was injected an hour later, when consciousness returned, and another 10 c.cm. in two hours. Improvement continued rapidly, and two further injections of picrotoxin 10 c.cm. given at five-hourly intervals were probably unnecessary. The patient received 50 c.cm. of picrotoxin in all. She made a good recovery in her mental state and was discharged.

CASE 2.—A female, with recurrent melancholia, had depression with suicidal thoughts. She was in good bodily health. She had had a previous narcosis without any untoward result. She collapsed on the third day of treatment, after having received altogether gr. 75 of medinal and gr. 15 of luminal, and the result of treatment with picrotoxin (a total of 20 c.cm. being given) was equally excellent. Three days after the collapse narcosis was continued for fourteen days, with an excellent mental recovery.

CASE 3.—A female, aged 35, with recurrent mania, had an acute maniacal attack. She had had five narcoses previously, with good result. She was in good bodily health. During six days she received gr. 170 of medinal and gr. 34 of luminal. On the sixth day she collapsed and was unconscious, cyanosed, and stertorous, with a temperature of 102° F. This was due to the barbiturates and resembled "malignant" barbiturate poisoning (*Lancet* 1938). Routine treatment, as described above for case 1, with 30 c.cm. of picrotoxin injected intravenously, was given, and an immediate striking return to consciousness was observed, as in the previous two cases, but two hours later the patient again became unconscious, and a further 20 c.cm. of picrotoxin was required. Again there was an immediate return to consciousness. Four hours later picrotoxin 30 c.cm. was given, but the temperature rose to 104° F., pneumonia developed, and the patient died three days later. She had received 100 c.cm. of picrotoxin altogether.

CASE 4.—A female, aged 35, with acute mania and in good bodily health, collapsed on the tenth day of treatment, after having received gr. 245 of medinal and gr. 49 of luminal. She was unconscious, cyanosed and stertorous. Routine treatment with 10 c.cm. of picrotoxin solution produced an immediate return to consciousness, but 30 min. later she died suddenly from right-sided cardiac failure (verified postmortem).

CASE 5.—A female, aged 40, with recurrent melancholia, attempted suicide by taking gr. 100 of medinal. She had been in good bodily health. She became unconscious, cyanosed, and stertorous. Picrotoxin 10 c.cm. injected intravenously immediately restored consciousness and produced an improvement in the general condition. Further injections in six and twenty-four hours of 10 c.cm. each completed the recovery. She received 30 c.cm. of picrotoxin in all, and no routine treatment was given. This case was first diagnosed by finding barbiturates in the urine.

I have to thank Dr. D. N. Parfitt, medical superintendent of the Warwickshire and Coventry Mental Hospital, for permission to publish these cases.

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REVIEWS OF BOOKS

Recent Advances in Neurology

(4th ed.). By W. RUSSELL BRAIN, D.M. Oxfd, F.R.C.P., physician with charge of outpatients to the London Hospital; physician to the Maida Vale Hospital for Nervous Diseases. London: J. and A. Churchill. 1940. Pp. 364. 15*s*.

NEUROLOGY is now among the growing edges of medicine. Thanks to the physiologists, biochemists, and biophysicists, it has taken on a dynamic aspect which finds accurate reflection in this new edition of a familiar friend. So rapid have been the advances in the last six years that the whole book has had to be rewritten. A new chapter on headache summarises briefly the work of Pickering on histamine headache, the methods of preventing lumbar puncture headache, and the ergotamine-tartrate treatment of migraine. Foerster's mapping of epileptogenic cortical areas is described, and this leads on to an excellent chapter on the electro-encephalogram. The work of Grey Walter on cerebral localisation and on grand and petit mal is discussed in full. In the chapter on the functions of the frontal lobe, psychiatry and neurology join hands. It seems certain that partial or complete frontal extirpation produces changes in affective state, usually in the direction of euphoria, though sometimes towards depression. The higher intellectual processes are also impaired, though attention, memory and grasp are not upset. These findings are of great interest just now, for an operation in which maceration of the frontal lobe is performed is achieving a certain popularity in the United States for the treatment of severe obsessional disorders. Dr. Brain gives 14 well-deserved pages to the hypothalamus. He has, too, much of interest to say on sleep, narcolepsy, neurotropic viruses, prostigmin, the biochemistry of the muscular dystrophies, the vitamins in neurology, and a host of other fascinating subjects. There is a clarity, simplicity and objectivity about the book which makes even the fairy-tales of medicine credible.

Synovial Membrane and Synovial Fluid

With special reference to arthritis and injuries of the joints. By DAVID H. KLING, M.D., assistant professor of orthopedic surgery and chief of arthritis clinic, White Memorial Hospital, Los Angeles. London: Baillière, Tindall, and Cox. Pp. 284. 25*s*.

THE value of a monograph (as of a review) depends on the ability of the author to appraise the work of others; it is seldom as satisfactory as an account of original work. When, in addition, it involves disciplines as widely ranged as embryology, physiology, morbid anatomy, biochemistry, bacteriology, and practical medicine, appraisal obviously becomes increasingly difficult. The industrious author of this first and only monograph on synovial fluid and synovial membrane has succeeded in covering his large field adequately. It is a pity, however, that Dr. Kling has not taken this opportunity of correcting some of the errors in the American printing of May, 1938. A few of the typographical errors have admittedly been corrected, but the reference, for instance, to "Curtis and Brandenburg" is still wrong. There are also numerous dogmatic statements which the reader would do well to doubt until evidence is produced in their favour—e.g., "the structural and functional changes (in degenerative joint disease) are at least in part due to a lack of proper lubrication and protection of the articular cartilage. This can be explained as an inadequate development of secretory areas which elaborate a synovial fluid inadequate in quantity and quality"; and "not the plasma colloids but mucin is the first safeguard for the maintenance of the high alkalinity of normal synovial fluid." The mood in which to approach joint physiology is the subjunctive, but a flat denial may be given to the last statement.

In part 1 Dr. Kling emphasises the mucin secretory function of the synovial membrane. While this seems likely, neither the published reports nor Dr. Kling's photograph of three cells with mucin granules stained by toluidine blue offer convincing proof. Indeed, it was only in August, 1938, that the chemical constitution of mucin was established by Meyer. Acceptable evidence of secretion would be the chemical identification of mucin in metastases of the malignant synovioma, of which no details are given. The synovial fluid is discussed in part 2 with 19 tables, and in part 3 the character and reaction of this fluid in various pathological conditions is described. Too many references appear to the "sac-and-tube reaction." This, the author explains, is a qualitative test for mucin and is positive in 100 per cent. of normal synovial fluids; yet he writes: "in (traumatic) effusions aspirated within 24 hours after injury, the sac-and-tube precipitation reaction for mucin was found to be positive. This indicates that, due to the irritation of the hæmarthrosis, hypersecretion of the synovial fluid sets in almost immediately." Part 4 will be of most immediate value to the clinician. The author's advocacy of joint puncture is fully supported by the preceding chapters, and is a procedure which should be more widely practised, both for diagnostic and therapeutic purposes. This is perhaps the most important aspect of the book.

Early Diagnosis of the Acute Abdomen

(8th ed.) By ZACHARY COPE, M.D., M.S. Lond., F.R.C.S., surgeon to St. Mary's Hospital, Paddington. London: Humphrey Milford, Oxford University Press. 1940. Pp. 257. 10*s*. 6*d*.

THIS book needs no introduction to the profession, for it has enjoyed a wide popularity since it was first published nearly twenty years ago. This edition differs from its predecessor only in small verbal changes and additions and the inclusion of three more X-ray photographs. That no more serious alterations than this have been needed is sufficient testimony to the solid worth of the book, and it is not easy to see how it could be improved. In the next edition, however, it might be worth while to include a short section on the mechanism and interpretation of abdominal pain.

L'anoxémie, ses effets

Son traitement l'oxygénothérapie. By LÉON BINET, professor of physiology in the Faculty of Paris; MADELEINE BOCHET and M. V. STRUMZA, assistants in the faculty. Paris: Masson et Cie. 1939. Pp. 96. $0·60.

THIS little book is for the most part a record of experiments in which dogs anæsthetised with chloralose were made to breathe mixtures containing less than the normal amount of oxygen but at normal barometric pressure. The animals react by hyperpnœa, tachycardia and elevation of blood-pressure. Reaction cannot persist indefinitely when the percentage of oxygen is greatly diminished: the amplitude and rate of respiration eventually diminish and the blood-pressure falls. In animals deeply anæsthetised, breathing fails before the heart ceases to beat, but this is not always the case, and the heart may fail before the respiration when anæsthesia is less

profound. This experimental technique has been used to study the hæmatological and biochemical reactions to anoxia and the variations in resistance which can be produced by pharmacological or biological means. The dog reacts to acute anoxæmia by contraction of the spleen and erythrocytosis. Resistance is much diminished by agents such as anæsthetics which depress the respiratory centre, but whereas it is increased by drugs such as ephedrine and benzedrine which encourage splenic contraction, it is not appreciably improved by stimulants such as caffeine, the camphor group or lobeline. The histological lesions produced in mice and guinea-pigs by atmospheres containing an excess of oxygen are then described. It is doubtful whether any of these observations, particularly the last, can be translated directly to the domain of human pathology, and the results will probably be most useful to anæsthetists, who cannot be too familiar with the additive effects of narcotics and anoxæmia. The monograph finishes with a brief review of methods of administration of oxygen and the use of breathing machines.

Midwifery

Principles and practice for pupil midwives, teacher midwives, and obstetric dressers. By R. CHRISTIE BROWN, M.S. Durh., F.R.C.S., F.R.C.O.G., obstetric surgeon, City of London Maternity Hospital and Plaistow Maternity Hospital; and BARTON GILBERT, M.D. Lond., F.R.C.S., M.R.C.O.G., second gynæcologist, Metropolitan Hospital. London: Edward Arnold and Co. 1940. Pp. 796. 15*s*.

THIS admirable manual for pupil midwives begins with a hundred pages on general science, anatomy and physiology, in the belief that the potential midwife will learn and understand her midwifery better if she has even a slight knowledge of the underlying principles. The field of midwifery is covered clearly and adequately, although briefly, and the parts played by midwife and doctor are clearly differentiated. In future editions perhaps forceps delivery and tentorial tears might be more fully considered and perversions of appetite not be quoted as the sole example of nervous stress in normal pregnancy.

Thorpe's Dictionary of Applied Chemistry

(4th ed.) Vol. III (*Chemical Calculations—Diffusion*). By Sir JOCELYN THORPE, D.Sc., F.R.S., emeritus professor of organic chemistry in the University of London at the Imperial College of Science and Technology; and M. A. WHITELEY, D.Sc., F.I.C., lately assistant professor of organic chemistry, Imperial College of Science and Technology. London: Longmans Green and Co. 1939. Pp. 608. 63*s*.

THIS volume seems to be concerned more than its predecessors with applied as distinct from pure chemistry, but this may be merely an alphabetical accident. Therapeutical chemistry is well represented by articles on chloramine-T, chrysarobin, cocaine, cod-liver oil, colchicum, croton oil and curare, among others, while the 51-page account of the cinchona alkaloids deserves special mention. The biochemist will appreciate the contributions on chlorophyll, cholesterol, choline, creatine, creatinine and cytochrome. The authoritative articles on chemical warfare and chemical warfare defence, and those on the explosives cordite and cyclonite, are sadly well timed. The first of these deals with the use and manufacture of war gases, their physiological effects and the concentrations required to produce them. It will be a surprise to many that Lewisite has not been used in actual warfare. A considerable part of the article on defence discusses respirators used to combat gas hazards in industry. The article on chemical calculations describes the technique of triangular charts, nomograms and adjacent scales, aids which might be put to greater use by workers in the biological sciences.

1939 Yearbook of Urology

Edited by J. H. CUNNINGHAM, M.D., associate in genito-urinary surgery, Harvard University post-graduate school of medicine. Chicago: The Year Book Publishers; London: H. K. Lewis and Co. 1939. Pp. 443. 12*s*. 6*d*.

THIS yearbook has now established its claim to a place on the bookshelves not only of urological specialists but of general surgeons and physicians as well. There has been a falling off this year in the contributions on urology from many European countries, so that America, and more especially the United States, has supplied the bulk of noteworthy articles. The high spots are the use of the sulphonamides in urinary infections and some important work on the kidney, more particularly on its physiology and pathology. Little has escaped the eye of the editor, and he cannot be accused of paying less attention to foreign literature than to the home production. But 1939 seems to have been singularly unproductive in the field of urology.

Pharmacology, Materia Medica and Therapeutics

(15th ed.) By BIRENDRA NATH GHOSH, M.B.E., F.R.F.P.S., F.R.S.E., professor of pharmacology, Carmichael Medical College, Calcutta. London: H. K. Lewis and Co. 1939. Pp. 763. 15*s*.

THIS book, first published in two volumes in 1901 and 1903, has had a succession of able editors. Since the last edition in 1936 there have been many valuable additions to the therapeutic armoury—the sulphonamides in streptococcal and other infections, the salts of mandelic acid in septic conditions of the genito-urinary passages, and nicotinic acid in pellagra, to name but a few. These all receive adequate discussion here. Professor Ghosh has added some tracings illustrating the pharmacological action of drugs, and throughout he has been at pains to set forth the practical applications of pharmacology to scientific therapeutics. If any criticism could be levelled against his book it is that it contains too much detail for the medical student, but as a work of reference it will be a most useful adjuvant to a course of lectures.

The Riddle of Woman

By JOSEPH TENENBAUM, M.D. London: John Lane, The Bodley Head. 1939. Pp. 477. 12*s*. 6*d*.

THIS volume of the International Library of Sexology and Psychology covers an ambitious field, surveying woman from many aspects—mythical, anthropological, historical, biological and psychological. Though the ultimate riddle remains unsolved Dr. Tenenbaum throws much light in dark places. He discusses woman as wife, bride, mistress, divorcee, widow, virgin, spinster, mother, grandmother, mother-in-law, angel, gossip, criminal and witch. There are separate chapters on physiology and psychology, the sex urge, the development of marriage, the evaluation of beauty, and woman in industry, commerce and the professions. The author quotes extensively from diverse sources: from the Koran, King Hammurabi of Babylonia and Juvenal on the one hand, to Freud, Briffault and Havelock Ellis on the other. The book is almost too replete with facts, some of the psychological jargon is difficult to follow, and the multitude of rather forced epigram is apt to be irritating. But though the going is sometimes heavy the doctor will find his expenditure in concentration well repaid in the help the book will give him in coping with his female patients.

THE LANCET

LONDON: SATURDAY, MARCH 30, 1940

HOLIDAYS AND COMMON SENSE

"...while all things else have rest from weariness?
All things have rest; why should we toil alone,
We only toil, who are the first of things"

(*Tennyson's Lotos-Eaters*)

Last week-end when everyone else was holiday-making ten thousand miners in the employ of the Bolsover Colliery Company forwent two days of their usual Easter break for the sake of replenishing the national supply of coal and the press congratulated them on their patriotic spirit. More than that, the same miners are said to have resolved to surrender part of their summer holiday and to work on alternate Saturdays, receiving instead their quota of the holiday savings fund. It is a curious anomaly of our present-day social structure that the people who do the hardest physical work are considered to need either very short holidays or none at all. Added to this they are required to work longer hours than sedentary workers. Strange, is it not? For the list of dangers to which the miner is exposed reads, as we have lately pointed out,[1] like a litany—sudden death by explosion and fire and flood, by falls of earth and shaft cages; asphyxiation by gas, electric shock and entombment—each year two in every eleven earn compensation for injury sustained or diseases contracted. It is these men who have been adjured, nay persuaded, to surrender their leisure. "Miners give a lead" was the title of one leading article. There must be some reason for this obvious lapse from common sense; in part at least it arises from a perverted instinct of self-preservation, in a struggle for existence where the stronger or more cunning have exploited their weaker or more unselfish neighbours.

Happily signs are not lacking of the growth of a social conscience, stimulated no doubt by legal measures and still more by the discovery that in the long run it improves the balance-sheet to look after the health and welfare of workpeople. Nearly everyone who has thought about the matter has agreed that a period of physical or mental activity should be followed by an adequate period of rest and recreation wherein the vital forces may be renewed. Poets, philosophers and scientists have stressed the fundamental rhythms in life and nature, and the experience of the ages has been distilled into the proverb "All work and no play makes Jack a dull boy." Those who think in terms of the equation, output equals number of workers multiplied by time spent in mine or factory, have forgotten the last war. Longer hours and fewer holidays produce more accidents, more lost time, less coal or shells. On page 43 of the final report on the health of munition workers, issued in April, 1918, we read: "The committee consider it most important that the ordinary factory holidays should be maintained"; and this weighty judgment (we cite below the signatories [2] to the report) was fortified by a single sentence from a trade-unionist: "If once in every two or three months a man could have two or three days off it would prove the finest medicine, much better than a bonus as extra pay." After this it seemed almost superfluous to add any evidence of the beneficial effect of holidays on health and output. In one investigation Dr. VERNON found that after a week's holiday at Easter the hourly output in the factory went up from 123 to 134 and remained steady for the next eight weeks although the hours of work were slightly greater than before Easter. After a week's holiday at the end of August the output went up again to its May–June level, and in October when the Government ordered four days off work another rise set in and continued until just before Christmas when the output reached the astonishing figure of 177. "The workers, refreshed and more vigorous, unconsciously start work" said Dr. VERNON "on a higher level of speed and maintain that level permanently, whereas a reduction of hours unaccompanied by a holiday—i.e., by a chance of breaking through settled habits of work—is generally very much slower in conducing to the desired reaction."

Time presses and while the summer is still before us something practical must be done, for while the principle of holidays—sometimes long holidays—for the sedentary worker is firmly established, the holidays-with-pay movement for the manual labourer is only in its infancy and has still to wear down the tendency to regard holidays as an undesirable interference with production. In Coventry last September the two days' holiday which was to be granted under the spread-over arrangement was cancelled for engineering workers. On the other hand shortly after the war began the wool-textile employers agreed to pay their operatives for a week's holiday in 1940 and the Bakery Trades Board proposed a scheme for holidays with pay. But careful planning will be required to avoid the congestion on road and rail, the overcrowding and enhanced prices, of the holiday concentrated in a few weeks at the height of summer. For this reason it is essential that holidays should be spread over the months from May to October. The committee on workers' holidays set up by the Industrial Welfare Society under the chairmanship of Lord AMULREE is now appealing to local authorities, to employers and to the representatives of the workpeople to get together and discuss local arrangements for a spread-over. Some of the largest industries have

1. *Lancet*, 1939, 1, 35.

2. George Newman (chairman), Thomas Barlow, Gerald Bellhouse, A. E. Boycott, J. R. Clynes, Edgar L. Collis, W. M. Fletcher, Leonard Hill, Samuel Osborn, Rose E. Squire, May Tennant.

already made a habit of staggering holidays, as it is inelegantly called, but engineering and other works have simply closed down for a week in August. This is the time to consider plans that will make for the least dislocation of work and the most opportunity of family reunion. Married women workers with dependent children need special consideration; the Board of Education has relaxed its ban on a child's absence from school for a week to join the family holiday. With good-will all round something more than a temporary expedient will have been achieved. Common sense will have entered into holiday planning.

SCABIES ON THE INCREASE

ACCORDING to the official history half of the admissions to hospital from the armies in the field in the last war were due to lack of cleanliness and vermin. Scabies was by far the commonest of such diseases, and only a tenth of the cases were uncomplicated, for it is by its complications—boils and secondarily infected sores—that scabies does most harm. The scratching caused by the severe itching assisted the spread of the lice-borne diseases, trench fever, relapsing fever and typhus. In London, after a sharp rise in the two years after the last war, the number of cases of scabies among school-children fell, until in 1925 only 2000 were recorded. Since then the number has risen, in the last few years rapidly, and in 1938 it reached 14,000. Increased incidence is reported from all parts of the country and cannot as yet be explained. The itch mite is delicate and cannot gain a hold on the skin when proper cleanliness is maintained; in clothes it is probably killed by simple washing, but where there is overcrowding and washing is difficult the disease may spread fast. In all our cities we keep a reservoir of infection among a few adults, poor either materially, physically or mentally, from which are fed the streams of children to the cleansing centres. Years of effort in school hygiene have not touched this source of contagion and it will never be removed until medical officers of health have power to inspect, and if necessary cleanse, such adults. The whole problem of body vermin would then be solved. In the control of scabies there are three points of importance: early and accurate diagnosis, since simple scabies is a disease easily and quickly cured; efficient treatment of the whole family at the same time; and disinfestation of the clothes and bedding.

Sulphur ointment is the traditional, though inefficient, remedy still mentioned in most text-books of dermatology, though, as is well known, it often causes a dermatitis worse than the disease it is intended to cure. Twenty years ago LOMHOLT [1] introduced to England from Denmark a modified sulphur ointment which gave far quicker and more certain results and produced less dermatitis. In 1937 KISSMEYER [2] brought us, again from Denmark, an even more successful treatment, a paint of benzyl benzoate, soft soap and isopropyl alcohol in equal parts. Industrial methylated spirit incidentally is much cheaper and as effective as isopropyl alcohol. The patient is thoroughly scrubbed and soaks himself in a hot bath, after which the lotion is painted on the skin and allowed to dry. A bath next day with a change of clothes completes the treatment. The paint may be applied over sores without harm, though it may sting a little, and subsequent dermatitis is rare. In a recent trial 140 out of 144 children were cured with one application and were each away from school for two days only, whereas 95 children treated at the same time as a control with the Danish ointment needed an average of five treatments each and were away from school for an average period of a fortnight; only 2 were cured with a single treatment. The efficiency of the benzyl-benzoate treatment has been proved beyond doubt—8000 cases have been successfully treated in Copenhagen—yet we learn from the responses to a questionnaire issued by the Leicester county borough that of eighteen large local authorities only three were recently using it and ten were still using the old sulphur ointment.

1. Lomholt, S. *Lancet*, 1920, **2**, 1251.
2. Kissmeyer, A. *Ibid*, 1937, **1**, 21.

KELOIDS

THERE are few things more disheartening to the surgeon or his patient than the development of a keloid in the scar of an operation that has otherwise been a success. After a plastic operation it is a tragedy. Keloids are most often seen in the slowly healed areas of third-degree burns, but they may arise in the scars of injury, operation or vaccination. Some seem to come spontaneously, particularly on the front of the chest, and it is in these that the claw-like processes springing from the main mass are seen, and give the name to the condition. Since these probably start in some minor injury or acne pustule, it is not necessary to seek a separate pathology for them. The essential histological change is a tremendous overgrowth of collagenous fibrous tissue in the corium, which seems to develop around the smaller blood-vessels. The papillæ of the skin disappear and the surface becomes smooth. The scar is raised above the surface and is red, tense and shiny. Later the vessels atrophy, and the keloid tends to become paler and less evident.

Why do these changes develop in some scars and not in others? Some people are particularly prone to keloid-formation, and the cautious surgeon may think it worth while to make a preliminary incision in some unexposed part to test the tendency, though different scars may behave differently in the same person. Scars that run across the lines of cleavage of the skin are more readily affected than those parallel to these lines, and this probably explains the keloid developing in one limb of an L-shaped incision. (It should be noted that some of the published diagrams of the lines of cleavage are incorrect.) A striking fact is that keloids are six times more common in the dark than the light skinned races. Disorders of endocrine glands, increased calcium in the blood, vulnerability of the elastic tissue, and congenital

disposition of the connective tissue to hyperplasia have all been considered important factors. FILIPS [1] says that keloids can be produced in anyone, quite apart from inborn tendency, if a sufficient amount of the reticular layer of the cutis is destroyed by the high-frequency current. Lesser and more superficial injuries do not produce this reaction, while injuries penetrating the subcutaneous tissue produce a greater reaction. He believes this is because in the deeper injuries a greater number of small blood-vessels are stimulated to proliferate. Similar changes may be produced by caustic acids or alkalis, salts of heavy metals, and thermocautery or electrocautery, if enough of the reticular layer is destroyed. The fact that keloids are so common in the healed areas of large and deep burns makes it not unlikely that infection plays a part in their production, for in the process of healing hypertrophic granulation tissue is characteristic. In areas from which razor grafts have been taken healing may be perfect in one part while in another where healing has been delayed a keloid may develop. It is probable that some degree of infection is present in many wounds that are thought to be healing by first intention. MELENEY [2] has shown that if a careful postoperative count is taken it will be found that from 15 to 30 per cent. of wounds thought to be "clean" show evidence of infection. He has also found hæmolytic streptococci in the throats of about a quarter of those present in operating theatres, and the work of PAINE [3] and WELLS and WELLS [4] proves how easy it is for a wound to be subjected to droplet infection from such a source. HART [5] has recorded the difficulties in eliminating bacteria from operating theatres, short of sterilising the air. If infection is of any importance the occasional development of a keloid is not to be wondered at, and this is a further reason for consummate care in operating.

Simple surgical excision and suture is useless in the attempt to get rid of one of these blemishes. The new scar will certainly develop another keloid and a worse one because of the tension engendered by the excision. It may occasionally be necessary to replace a large keloid by a graft, but only a direct flap or tube pedicle is any use, for with a thinner graft too much fibrous tissue is deposited in the process of healing. After such an operation radiation must be employed from the start, for this is the only agent that seems to control fibrous-tissue deposition, and the newly formed scar is particularly radiosensitive. Radiation is often of value in reducing the size and colour of a keloid that is unsuitable for surgery, but long-standing scars do not respond readily to radiation, and great care is necessary to avoid overdosage, for a radiation burn is much more serious than a keloid. Radium and X rays are both used, but FILIPS thinks radium dangerous, and uses it only for small children who cannot sit still enough for X-ray treatment. For the scars following excision of a keloid he uses five erythema doses spread over nine weeks, employing 125 kV, with a 5 mA current, and 3 mm. aluminium filter. For large keloids following healing by secondary intention he uses half an erythema dose weekly for eight weeks. Very large keloids may require longer treatment.

1. Filips, L. *Med. Rec.* 1939, **150**, 379.
2. Meleney, F. L. *Surg. Gynec. Obstet.* 1934, **59**, 358.
3. Paine, C. G. *Brit. med. J.* 1935, **1**, 243.
4. Wells, W. F. and Wells, M. W. *J. Amer. med. Ass.* 1936, **107** 1698, 1805.
5. Hart, D. *Arch. Surg., Chicago*, 1937, **34**, 874.

WHEN THE SKIN DEFENCE IS BREACHED

IT is nearly a century since IGNAZ SEMMELWEIS watched his friend KOLLETSCHKA die of septicæmia after pricking his finger when making an autopsy and it flashed into his mind that it was the same disease as he had seen killing puerperal women by the thousand in the Vienna lying-in clinic before he induced students and midwives to wash their hands with chlorinated lime. That was the first clue to the curious defencelessness of the human body, otherwise so well protected, when its protective envelope is broken. Within its intact skin and mucous membrane the body can laugh at the germ life around it; break this pellicle and the laugh is on the other side. The germ runs riot in tissues which have had no previous experience of its attack. Since SEMMELWEIS posed this problem JOSEPH LISTER has shown surgeons how to solve it with a large measure of success for the wounds they themselves inflict at their own time and place. But in the accidental wound of the post-mortem room and in impromptu injuries of high speed on the road or high explosive from the air the die is still heavily weighted in favour of the germ. For the moment at least there is a lull in the wholesale infliction of wounds and the time seems opportune to consider what is known about the prevention and treatment of wound infection. On p. 608 Mr. W. H. OGILVIE begins a series of articles with a formidable list of questions which are still open. In following issues Colonel L. E. WHITBY will set out the fundamental pathology of ideal healing and what stands in its way, Dr. ROBERT CRUICKSHANK will discuss sources of infection and general preventive measures, leaving Prof. L. P. GARROD to deal with antiseptics and Major G. A. H. BUTTLE with chemotherapy. A review by Mr. OGILVIE of surgical methods in prophylaxis and treatment will close the series, which, it is hoped, may serve as a refresher course to those who in the event of more active warfare will have to deal, at home or overseas, with this major problem of wound infection.

Miss RUTH DARBYSHIRE, R.R.C., who succeeds Dame Joanna Cruickshank as matron-in-chief of the Red Cross war organisation brings to her task much experience and knowledge of nursing in peace and war. Before holding for twelve years the matronship of University College Hospital she had been in charge of the Derbyshire Royal and St. Mary's, Paddington, and had spent six years in India as head of Lady Minto's nursing service. During the last war she was principal matron of the 2nd London General Hospital. She has been vice-chairman of the General Nursing Council and she was, we gratefully recall, a most useful member of THE LANCET Commission on Nursing.

ANNOTATIONS

THE NATIONAL LARDER

THE storage of food may have been the beginning of capitalism, but certainly, under Joseph of Egypt, it was the beginning of state socialism. And today, several thousand years later, we have the Department of Scientific and Industrial Research stepping in to advise food importers how to preserve their foods to the best advantage, though not doing it for them, as Joseph did. Theoretically the old-fashioned economists would have expected this knowledge to have been acquired without state intervention, but apparently the stable if not generous conditions of state employment attract the scientific research worker whereas the pinchbeck and uncertain conditions of industrial research do not. The report of the Food Investigation Board for 1938 [1] points out with some natural pride that "In the brief period of 5 years since the method [i.e. of storage of chilled beef in air 'enriched' to a controlled extent with carbon dioxide] was introduced, the exports to us from Australia and New Zealand of chilled beef have increased nearly tenfold to a combined annual figure of 850,000 cwt. Since chilled beef has recently commanded a premium over frozen beef of about 1*d.* a pound the increased value of this meat is of the order of £400,000." That is certainly a remarkable achievement. It has made more of a satisfactory food available in better condition in a country which will never be able to supply all its wants in this direction. We hope that a fair proportion of that £400,000 has flowed back into the coffers of applied food research. Nothing is said about a reduction in price of chilled beef to the populace, but presumably that may happen as the result of the research, owing to economic laws.

A more important research from the point of view of medicine and dietetics is that undertaken on behalf of the government of Palestine on the wastage of oranges during transport. One of the desiderata of a good diet is an adequate supply of vitamin C, especially during the winter months. The orange is the most convenient and stable source of supply, for we cannot grow enough watercress for that purpose in this country. Anything which decreases the rotting of oranges by green mould is going to increase the supplies of vitamin C at a cheap rate. So far as the work has gone we learn that the November fruit wastes more rapidly than the March fruit (which is a pity) and that wastage can be lessened by ventilation and by low temperature. Wrapping in papers impregnated with hexamine and *o*-phenylphenol helped to prevent rotting. The report also notes that King Edward potatoes lifted in September and October have the high vitamin-C value of 43–45 mg. of ascorbic acid per 100 g. and that this amount falls with storage at 10° C., reaching asymptotically by the next April a figure of 10 mg. Six-month old potatoes are therefore not to be despised as sources of vitamin C, having about a third or a quarter that of oranges and somewhat less than that of the Jamaica banana sold in this country.

A mass experiment was undertaken on the gas storage of Cox's orange pippin, and at the end of five months' storage an apple was released which had most if not all of the qualities of a freshly picked apple. Since, however, the Cox's orange pippin contains but little vitamin C, and few other protective qualities, the experiment is of more interest to gastronomes than to dietitians. We learn that July is the best month for kippering herrings, that the ripening of pears can be controlled so that they do not all ripen at once, that late and early apples should not be stored together, and that potatoes make use of a triose phosphate in the oxidation of carbohydrate, just as if they were yeasts or frogs' muscles.

The report demonstrates the immense importance of liaison between academic research in biochemistry and the practice of supplying the nation with sound food. This work will undoubtedly continue to advance and both the research and the research workers deserve a satisfactory subsidy.

1. H.M. Stationery Office. 1939. 4*s*.

PICROTOXIN IN BARBITURATE POISONING

IN spite of the new Poisons and Pharmacy Act, suicides still find the barbiturates convenient for their purpose, and this fact together with the increasing use of these drugs for producing long narcosis in psychiatry provides a constant supply of toxic cases for treatment and study. Sixty-five years ago Crichton Browne suggested the trial of picrotoxin for chloral-hydrate poisoning and in 1931 Kline, Bigg and Whitney [1] reported that this powerful convulsant was more effective than strychnine in barbitone poisoning in animals. Since then about a dozen cases treated with picrotoxin have been reported, and the results were reviewed in the *Presse Médicale* for Jan. 10. On another page Gillman describes the use of picrotoxin in four cases of poisoning arising during a hundred narcoses for psychiatric purposes and in a fifth case of suicidal poisoning. Unfortunately the treatment itself is not without danger, doses of picrotoxin large enough to be effective being accompanied by toxic symptoms, and in particular by grave secondary cortical depression. Nevertheless, picrotoxin is a real and fast-working antidote to the barbiturates, and the attendant risk may well be justified. Lately Metrazol has been suggested as an alternative; this drug is said to be slightly safer in that secondary depression makes its appearance only after a dosage sufficient to cause convulsions.

OCCIPITO-POSTERIOR PRESENTATIONS

WHAT is the truth about labour in cases of occipito-posterior presentation? That these give rise to anxiety and difficulty is shown in the reports of any maternity hospital, where about half of the cases admitted as "failed forceps" are found to be occipito-posterior with an improper application of instruments. Most of these must arise from a faulty understanding of labour. In a series of 2130 consecutive vertex deliveries, of which 1020 were occipito-posterior, Calkins [2] found that usually little was to be feared if the patient was treated on expectant lines without undue interference. In 95 per cent. of his patients spontaneous rotation took place and the fœtal mortality was only 2·8 per cent. These findings support the customary teaching of conservative midwifery. Uterine inertia, one of the banes of the obstetrician in these patients, was only present in 8·6 per cent. and here Calkins seems to have been fortunate for on an average labour was only 1½ hours longer in the posterior than the anterior cases. This apparent freedom from inertia may have been partly due to the fact that all his patients were examined vaginally early in labour, and hence cases which might have been classified as anterior if examined later were

1. Kline, E. M., Bigg, E. and Whitney, H. A. K. *J. Amer. med. Ass.* 1937, **109**, 328.
2. Calkins, L. A. *Amer. J. Obstet. Gynec.* 1939, **38**, 993.

included. No less than 276 rotated before full dilatation of the cervix; early examination certainly explains the astonishing frequency of posterior cases in the series (50 per cent.). If inertia does occur it is likely seriously to prolong labour—up to 24 hours or longer. Unfortunately no analysis of fœtal mortality is given by Calkins, so one is left wondering whether he finds it chiefly in cases with inertia.

A somewhat different impression is given in a paper by Proctor and Dickinson [3] based on 106 private patients. They adopt a less expectant attitude, and in only 39 of their cases did spontaneous rotation or spontaneous delivery in the posterior position take place. In ordinary clinical practice the truth seems to lie between these two expressions of opinion. Treatment should therefore be on conservative lines with adequate help in the first stage by sedatives, and interference in the second stage should be dictated by arrest of advance in the presence of good contractions. It is impossible to be dogmatic as to how long the second stage should last before we should interfere; to decide as do Proctor and Dickinson that after a certain number of hours one should rotate and put on forceps must sometimes increase the fœtal risk through insufficient moulding and lead to a more difficult forceps operation. In neither of these papers is delay in the first stage discussed fully. This is a complication which taxes the patience of the mother, the relatives and the obstetrician, and contributes appreciably to the infantile mortality. As long as it is not present occipito-posterior labours can be approached, as Whitridge Williams said, with entire equanimity.

SULPHANILAMIDE IN THE LOCAL TREATMENT OF WOUNDS

THE local application of sulphanilamide in infected or potentially infected wounds has not been encouraged. These compounds, it has been pointed out, are not true antiseptics. They show bactericidal effects on the hæmolytic streptococcus in vitro only when the organisms are scanty. There seems, however, to be no general agreement about the way in which they act in the body. Evidence has been brought forward by Wolff and Julius [4] that sulphanilamide acts on organisms only when they are actively multiplying. This would explain why it is more effective in acute infections than in chronic. If this suggestion is correct there is no logical reason why the compound should not be used locally. Excellent results have in fact been claimed by Jensen, Johnsrud and Nelson [5] in the treatment of potentially infected compound fractures and dislocations by local implantation of crystalline sulphanilamide. In 39 cases careful débridement, hæmostasis and closure of the wounds combined with complete reduction and immobilisation of the limb were supplemented by the insertion of 5–15 g. of solid sulphanilamide. Only 2 cases developed subsequent infection and in both of these the fractures had become recompounded owing to mismanagement. A series of 94 open fractures treated without sulphanilamide showed subsequent infection in 27 per cent.; 7 of these developed gas gangrene and in 5 amputation had to be performed to control the infection. Jensen and his colleagues also present some experimental support for this line of treatment. They fractured certain ribs in guineapigs and contaminated the wounds with cultures of *Staphylococcus aureus hæmolyticus*. The majority of animals in which solid sulphanilamide was implanted in the wound before closure survived without developing infection. When the sulphanilamide was omitted the majority developed suppurative osteomyelitis. In a further group it was shown that insertion of sulphanilamide into the tissues at a point remote from the infected site did not exercise any appreciable protective effect on the animal. With this local treatment, a higher concentration of the drug is maintained at the focus of infection than can be achieved by systemic administration. It is slowly absorbed, and as was demonstrated in two of Jensen's patients the maximum concentration in the blood-stream is reached after about 18 hours while a period of 60 hours is required for its complete disappearance. The question will naturally be raised whether so massive a local concentration of sulphanilamide is damaging to the tissues, and this should be investigated. Meantime it is encouraging to note that Wolff and Julius found that cultures of chick fibroblasts would grow as actively as control cultures in concentrations of sulphanilamide as high as 0·1 per cent.

3. Proctor, I. M. and Dickinson, K. *J. Amer. med. Ass.* Feb. 3, 1940, p. 381.
4. Wolff, L. K. and Julius, H. W. *Ann. Inst. Pasteur*, 1939, **62**, 616.
5. Jensen, N. K., Johnsrud, L. W. and Nelson, M. C. *Surgery*, 1939, **6**, 1.

GAS IN THE BOWELS

To the patient an excess of gas in the intestine may be anything from a social embarrassment to a source of severe discomfort. To his doctor it may be a sign of intestinal obstruction, of fermentation in the intestine or of one of the forms of "flatulent dyspepsia" which may be accompanied by circulatory phenomena such as faintness and palpitation or by difficulty in drawing a breath. Oppenheimer [1] found that in many of his patients gas in the bowel interfered seriously with satisfactory radiography. Preparation by active catharsis does not ensure freedom from distension, nor does a diet devoid of fermentable material and the administration of diastatic enzymes and hemicelluloses. Indeed most radiologists hold that the best way to prevent gas formation is to avoid all drastic measures of preparation and to evacuate any fæcal residues in the colon by a simple water enema alone. With normal contractility of the intestinal muscles large quantities of gas do not remain in the alimentary tract for long—they are got rid of upwards or downwards in the usual way. It is a common observation that patients with renal or biliary colic, duodenal ulcer and acute inflammation of the appendix or the pelvic organs are liable to gaseous distension. Oppenheimer observed it in fourteen patients with urinary diseases during intravenous pyelography about ten minutes after injection of the dye, and also when ureteral catheterisation was being carried out. Apparently there is an acute transient atony of the muscle of the intestinal wall in these cases, probably due to an inhibitory reflex. In the small intestines, besides widening of the lumen, the annular valvulæ conniventes become distinctly visible. In the dilated colon the haustrations become shallow and infrequent. A similar atony of the stomach has been observed at the onset of a migraine while taking a barium meal. Here the origin of the inhibitory stimulus is central; in other cases it may be peripheral—chemical, as in cholecystography and intravenous urography, or mechanical, as in distension of the renal pelvis with radiopaque fluid or oxygen.

Oppenheimer points out that though gaseous distension seems to follow acute intestinal atony, there is often little gas in the stomach or intestines in cases where distension is complained of, and it is evident that the contractility or tone of the intestinal muscle

1. Oppenheimer, A. *Surg. Gynec. Obstet.* January, 1940, p. 105.

plays an important part in producing the sensation of distension in non-surgical conditions. In surgical distension, obstructive or postoperative, pains set in when the recovering bowel first tries to expel the gas accumulated during a period of atony. An atonic bowel has its circulation interfered with and gas accumulates, but it is the tone of the intestinal muscle which determines the presence or absence of pain. Before beginning appropriate treatment therefore we should decide whether too much gas is being produced in a digestive tract otherwise normal or whether an irritable tract is responding by abnormal motor activity to the presence of gas. The two factors may at times be combined, but the old clinical distinction between meteorism—increased volume of gas—and flatulence—increased elimination of gas—is useful in guiding treatment.

"ARMY WANTS LAMBETH'S DOCTOR"

WE quote the headline of an article in the *Brixton Free Press*. Dr. A. G. G. Thompson, medical officer of health for Lambeth, being an officer in the Regular Army reserve, is to be called up to fulfil his duties in the Army. It is a matter of surprise that Major Thompson, like so many officers in similar circumstances who were called up at the beginning of the war, has not yet joined the British Army when his experience and knowledge of public health would have helped to solve the many problems which are bound to arise in the housing and feeding of a growing army of civilian recruits. Last September there was already talk of appointing a medical officer of health to work out such problems and Dr. Thompson would have been an ideal officer for the task. We are at war and should be making every effort to win it; not the least of these efforts is to produce a healthy and useful soldier. Lambeth borough council has thought only of the interests of its 250,000 citizens and has forgotten the more pressing claims of the B.E.F. Dr. Thompson has well served the citizens of Lambeth, and the borough health organisation could afford to lend his services to their and his army.

WHAT IS A DRUG?

IN an address to the Pharmaceutical Society on March 12 Dr. W. P. Kennedy, a member of the Poisons Board, raised the question of the meaning of the word "drug." He said that the knowledge of the narcotic or euphoric effects of certain plants is widespread in space as well as in time and all over the world people seek in them the unreal happiness and relief from strain which the modern psychologist knows as "the retreat from reality." Substances which produced such effects are, he said, known as drugs, though the term may properly be applied to all medicinal substances. Confusion in the public mind is shown by patients asking "Is this a drug, doctor? I don't mind taking medicine, but I will not be drugged"; nor is the misunderstanding restricted to laymen. What these people mean when they speak of a drug is a "dangerous drug," a term that is defined by law and has a specific connotation. Dr. Kennedy discussed the effects of a number of drugs of addiction—marihuana, mescal or peyote, a Mexican cactus that has lately found its way to Europe, the morphine derivatives and the barbiturates. He also described aspirin as a habit-forming drug, and quoted an American professor who had been struck by the tremendous amount of aspirin taken by women and young girls in this country. "It seems," he had said, "as prevalent as the gum-chewing habit with our young women." It is a far cry from hashish to aspirin and medicated wines but Dr. Kennedy said that many people delude themselves with the idea that when a wine is "medicated" it is somehow free from the stigma of "the demon rum." He mentioned a Scottish relative of his, a strong teetotaller, who has no objection to consuming port or sherry on the ground that they are funeral wines and therefore respectable.

RUBELLA

ONE of the tiresome features about an epidemic of rubella is that just when the doctor is beginning to regard it as an infection so trivial as to be negligible he is confronted with a patient who may fairly be said to be ill. Occasionally there is fever as high as 104° F., or a troublesome conjunctivitis lasting for several days. Respiratory catarrhs of greater or less severity are common and on another page Dr. Suffern describes a case of the much rarer sequel of toxic polyarthritis which is apparently uncomplicated by cardiac lesions. No age-group seems to be exempt and at least one case has been noted in a septuagenarian. Adenitis is by no means always confined to the cervical and occipital regions; enlarged glands are sometimes found in the axillæ, groins and popliteal spaces. Mild gastro-enteritis is occasionally encountered and so is desquamation, almost complete exfoliation being not unknown. Many people suffering from the disease, either through ignorance or because they do not feel ill enough, keep up and about and so spread the infection. Some boarding-schools, being fairly isolated communities, have decided to ignore the disease completely and have had no cause to regret this decision. With so long an incubation period isolation of contacts seems hardly worth while for a disease so mild and of such short duration. To ignore contacts but to isolate patients for a week from the appearance of the rash is probably the most practicable solution.

EXPERIMENTAL PRODUCTION OF INTRACRANIAL TUMOURS

AFTER many fruitless attempts in various laboratories to produce tumours of the brain by the insertion of carcinogenic substances success has been achieved. In spite of earlier failures Seligman and Shear,[1] working at Harvard University, now report the induction in mice of cerebral tumours by means of 20-methyl cholanthrene. Pellets of this substance were introduced through a burr-hole into the cerebral cortex of twenty young male mice of the "C_3H strain." Tumours were obtained in thirteen of the animals within periods ranging from 227 to 511 days, and in all of these the tumours developed at the site of inoculation and were extensive. In four examples the bone was invaded with the development of an extracranial extension. In two the tumour was histologically a fibrosarcoma apparently derived from the meninges; in the remainder it was a glioma. The gliomata are particularly interesting when compared with tumours of this class in human subjects. In one it appears to have been an astrocytoma; in the remainder the cells showed less differentiation, and from the descriptions and microphotographs it is clear that some are identical with and others closely akin to the common spongioblastoma (or glioblastoma) multiforme of the human cerebrum. Thus many of the cells are described as unipolar or bipolar spongioblasts, often showing a palisade-like arrangement about areas of necrosis, while the picture is completed by the presence of multinucleated giant-cells and mitoses. The tumours were as a rule ill-defined and showed invasive tendencies. Certain of the tumours were so undifferentiated that their classification is more difficult. Seligman and Shear are wisely

1. Seligman, A. M. and Shear, M. J. *Amer. J. Cancer*, 1939, **37** 364.

reluctant to assign names to them, but L. Alexander, in an addendum, labels them neuroepithelioma (2), ependymal tumour (1), oligodendroglioma (1) and pinealoma (1). The histological grounds for the identification of these types in the present material are, however, by no means adequate. Thus there is no information in the protocols concerning the presence or absence of blepharoblasts in the tumour cells, or, in the last example, evidence that the pineal body was involved in tumour formation. This, however, does not detract from the central fact that undoubted gliomata of malignant type have been artificially produced for the first time.

Cytologists will find in these experiments fresh evidence in support of the theory that the primitive cell types in the gliomata arise by anaplasia from more highly differentiated glial cells and not through the multiplication of embryological rests. It is to be hoped that future work will show how this latest success can be reconciled with spontaneous carcinogenesis. Inasmuch as the brain by reason of its position can hardly be influenced except through the blood-stream such a reconciliation might be expected to strike right to the root of the cancer problem. Two of the experimental tumours, one a glioma, have been successfully transplanted through several generations, and further work with this material may yield valuable information.

SCHAUMANN'S DISEASE

Lymphogranulomatosis is an overworked word these days. Tropical diseases claim a lymphogranulomatosis inguinale, and the malady long known to English physicians as Hodgkin's disease has of recent years become lymphogranulomatosis maligna to continental writers. In 1914 Schaumann described a syndrome called lymphogranulomatosis benigna consisting of a generalised enlargement of the lymph-glands associated with visceral changes and skin lesions (lupus pernio, Boeck's sarcoid), which is now usually referred to simply as Schaumann's disease. Later Schaumann described a lymphogranulomatosis metascrofulosa which accompanies or follows scrofulous enlargement of the lymph-glands. In *Acta Medica Scandinavica* for Feb. 13 M. S. Smith records a case of the metascrofulous variety with lupus erythematosis and unusual symptomless lung infiltrations, the latter resembling carcinomatous metastases. H. MacCormac gives clinical details of two middle-aged sisters exhibiting a typical picture of Schaumann's disease. G. Hochenleitter adds a third, and S. Berg completes the record with an example which raises the all-important question whether the disease is a definite entity or a form of anergic tuberculosis. Tuberculin tests are generally negative, while the histological picture in the lymph-glands, though suggesting tuberculosis in the epithelioid cellular response, is wanting in any manifestations of caseation or necrosis and is characterised by an unusually extensive fibrosis. Equally confusing are the radiographic appearances in the lungs, the shadows resembling a chronic miliary tuberculosis, secondary deposits of new growth or a pneumoconiosis. Lastly the widespread distribution of the lesions has caused different observers to emphasise different signs in what may possibly be one and the same disease—the sarcoid of Boeck, the osteitis cystica multiplex of Jüngling and the uveoparotitis of Heerfordt. It is small wonder therefore if both clinicians and pathologists seek for some unifying cause such as the ubiquitous tubercle bacillus. Ewing has said of lymphogranulomatosis maligna: "tuberculosis follows Hodgkin's disease like a shadow." In Schaumann's disease autopsies are rare and the tubercle bacillus, if present, is so sparsely scattered as to elude detection during life.

PHARMACOLOGY OF DIGITALIS

DIGITALIS is one of those drugs whose clinical value is undisputed but whose modus operandi is far from certain. Of the many theories that have been advanced to explain its action four have received particular attention: (1) slowing of the heart-rate; (2) increasing cardiac tone; (3) constricting the hepatic veins; and (4) reducing the size of a dilated heart. Each of these may represent part of the truth, but none is the whole truth. For instance, work on the effect of digitalis in heart failure with normal rhythm shows that the beneficial effects of the drug can be obtained without any appreciable slowing of rate.[1 2] Part of the difficulty in getting to the root of the matter has arisen from the tendency to apply the results of animal experiments to man when the effects may not be strictly comparable. This applies particularly to the theory of the constriction of the hepatic veins. Gold and Cattell [3] now advance the hypothesis that digitalis abolishes clinical heart failure by increasing the systolic force of the myocardium. In addition they present results which go to disprove many of the alternative theories. They conclude that the heart muscle is not overdistended in clinical heart failure, and also point out that the high venous pressure and the rapid rate in heart failure are not causes but results of this condition. In their experiments on cats they could find no evidence of constriction of the hepatic veins. With regard to the effect of digitalis on cardiac tone they point out that the heart may become smaller through various indirect mechanisms, such as reduced size secondary to improved force, diminished blood volume or other peripheral actions, and that if these possibilities are eliminated, as was done in their experiments, the heart has no tendency to shorten its diastolic length under the influence of digitalis even when its systolic force is increased several times. From the clinical aspect these results provide the most satisfactory explanation so far advanced of the mode of action of this drug. If they are confirmed the next step will be for the biochemist to investigate the method by which the increase in systolic force is produced. The possibility that the inorganic cations may play a predominant part has already been mooted.

We regret to announce the death in Lambeth Hospital, on Monday, of Dr. C. M. FEGEN, formerly chairman of council and later secretary of the London and Counties Medical Protection Society, aged 78.

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1. Luten, D. *Arch. intern. Med.* 1924, **33**, 251.
2. Marvin, H. M. *J. clin. Invest.* 1927, **3**, 521.
3. Gold, H. and Cattell, McK. *Arch. intern. Med.* February, 1940, p. 263.

Dr. C. Suffern sends us the following account of an unusual complication of German measles: A man of 47, after sixty hours of general malaise during which he felt shivery and ached all over, developed a typical rubella rash, with nasopharyngeal catarrh and sore throat. Next day he complained of tightness round the knees and twenty-four hours later the knees and midtarsal joints were swollen and painful. On the third day, when the rash had practically disappeared, the wrists were swollen and painful and on the fourth day the finger-joints of both hands were affected in the same way, so that the fists could not be completely closed. The joints cleared up rapidly, but a week after the appearance of the rash the patient still felt weak in the fingers, right wrist and left foot, and his right hand was still swollen, with a sensation of pins-and-needles, for a short time after he woke.

PREVENTION AND TREATMENT OF WOUND INFECTION

TREATMENT OF INFECTED WOUNDS

By W. H. Ogilvie, M.Ch. Oxfd, F.R.C.S.
SURGEON TO GUY'S HOSPITAL

It is remarkable that the problem of wound infection, which has engaged the attention of mankind since the dawn of history, should still be a topic of discussion and controversy. Seventy years ago it seemed to be solved: the causes of putrefaction and hospital gangrene had been discovered, the antiseptic method of wound treatment had triumphed, and infection was fast disappearing. Yet today the solution still eludes us, and we are even beginning to doubt whether much of the road trodden so laboriously may not have been in the wrong direction.

Infection did not greatly trouble the early surgeons, though the injuries of warfare were almost the only wounds they encountered. It may have been that the fatalists of those hard and religious days looked upon death as a matter for comment rather than analysis, it may have been that our ancestors retained much of the power of beasts to repair damage and combat the attacks of bacteria, but it is more likely that the proportion of gross infections was actually low. Wound infection or hospital gangrene first attracted attention in the eighteenth and nineteenth centuries, coincident with the founding throughout Europe of hospitals for the segregation and care of the sick and the development of planned operations, whose failure due to sepsis would naturally excite more comment than death on the field of battle.

The misery, the stench, the horror of a hospital ward in those days can be guessed from the writings of older surgeons, who indeed realised to the full the dangers that faced their patients, and did all that their knowledge would allow to alleviate the suffering they were powerless to prevent. Some came very near the truth. Randall in the seventeenth century postulated the existence of some minute and invisible animal or plant which caused the suppuration, but had not the means to prove his theories. Hunter brought his wonderful powers of observation and reasoning to the problem, and came as near its solution as his methods of investigation would allow. It was not till the invention of the compound microscope that the way lay open for Pasteur to identify the germs of putrefaction, and for Lister to suggest a way to combat them in the wards and operating theatre.

THE LISTERIAN RENAISSANCE

To Lister and his followers the world was full of germs that must be attacked—in the air round the operation, on the instruments, hands and clothing of the surgeon, in the operation field, and in the wound discharges afterwards. All germs were much alike, and except for a few striking examples like the bacilli of tetanus and anthrax the specific organisms responsible for infections of different types were not identified. Attention was concentrated upon killing the bacteria, and little was known of the defences of the tissues. Nevertheless by such a simple faith, and by such crude methods as the carbolic spray, a revolution was effected that has probably never been paralleled in the realm of human endeavour. Wound fever and gangrene disappeared from the hospitals; childbirth was no longer an ordeal to be dreaded; compound fractures, which had formerly ended in death or amputation, united nearly as readily as simple ones.

With the fear of infection abolished, the way lay open to the exploration of all parts of the body and the addition of a third method, reconstruction, to the two standard procedures of surgery, drainage and excision. Surgeons were quick to embrace the opportunities thus presented to them. Before Lister operations had been limited to the drainage of abscesses, amputations, the removal of stones from the bladder and the excision of surface tumours. Within fifty years of his first tentative demonstrations every cavity had been explored, nearly every operation that is known today had been performed or projected, and countless diseases formerly hopeless had been brought within the range of curative surgery.

The discovery of the bacterial origin of suppuration, and the period of intensive study and inquiry that followed, distracted attention for many years from the natural mechanism of defence possessed by the body, and threw into the shade the progress that had already been made in the conquest of infection by surgeons who were scrupulously clean in their operating and who favoured the natural reaction of the tissues by delicate handling at the time and rest afterwards. By such means alone Spencer Wells in London, Lawson Tait in Birmingham, and Spencer and Keith in Edinburgh were setting a new standard of safe and successful surgery, and showing results that would bear comparison with Lister's first tentative experiments in antisepsis. Gamgee, a leading exponent of the school of gentle surgery for which Birmingham had been known since the time of Robert Mynor a hundred years before, wrote in 1887: "The question is not one of antiseptics or no antiseptics, but of the form and proportions in which they should be employed in particular conditions. The great antiseptic is life. The living tissues have a natural preservative power which, if guarded and conserved by the surgeon on physiological principles, offers the surest guarantee for healthy repair which is only an adaptation and extension of normal nutrition." These words might have been written today.

It would be unjust to say that natural immunity and resistance to infection were forgotten during the Listerian renaissance for in this period the cellular changes of the inflammatory reaction were recognised, phagocytosis was described by Metchnikoff and the biological mechanisms of immunity were studied by Ehrlich, Almroth Wright and others. But surgeons still pictured themselves as knights whose mission was to rescue a nearly helpless patient from the hordes of bacteria that prowled on every side. Sepsis was a simple matter of the entry of germs into a wound; asepsis was the avoidance of germs, antisepsis the killing of germs that had arrived, disinfection the eviction of those already established. It was insufficiently realised that the chemicals employed in surgery were not so much antiseptic as antivital, that they damaged the defence mechanism as well as the invader. Pus came to be looked on as the symbol of evil, and house-surgeons were taught to change dressings as soon as they were soiled, to syringe sinuses till they were absolutely clean, to take out drainage tubes several times a day for sterilisation. The South African war did not shake the faith of the antiseptic school, for the casualties of typhoid greatly exceeded those caused by the enemy, and the wounds inflicted by the long mauser bullet in a country whose soil was almost free from pathogenic bacteria rarely became infected.

LESSONS OF THE LAST WAR

The war of 1914 to 1918 brought the problem of wound infection in its most acute form before a

generation of surgeons who had never seen hospital gangrene, but had grown up in the complacent belief that sepsis had been mastered, that its grossest manifestations, at any rate, belonged to the bad and buried past. All wounds suppurated and dressings and antiseptics seemed to be powerless. Septicæmia, pyæmia and gas gangrene made their appearance. The wards of military hospitals were filled with fever-stricken men. The compound fractures of war were as fatal as those of a century before, so that amputation became once again the commonest of operations.

At first the cry was "back to Lister," and those who directed surgical opinion sought by the use of stronger and stronger antiseptics applied at an earlier and earlier stage to stem the scourge. It was only by the failure of such attempts, and by bitter experience, that they learned that in infection the soil is no less important than the seed, and that healthy tissues have powers of dealing with bacteria which, if aided rather than hindered by the surgeon, can usually be relied upon to turn the scale against the invader. Thus it became the aim of the military surgeon to convert a war wound into a healthy one by removing not only foreign matter and dirt containing bacteria but dead and damaged tissues in which bacteria might multiply, and by obliterating dead spaces in which discharge might collect to form a culture medium. It was further realised that the state of surrounding structures and of the patient himself was nearly as important as that of the wound: that unless the injured parts were rested the tissues could not heal, and that without measures directed to combat shock, cold, and fatigue, fluid loss and hæmorrhage, the whole mechanism of repair was frustrated. In the last years of the war surgeons at the casualty clearing stations were able by excision and immediate suture, or in some cases by delayed primary suture, to avoid altogether the most severe infections in casualties brought to them within a few hours of wounding, and to secure clean healing in the great majority.

There remained the problem of the wounds already grossly infected when first seen, and of those in which infection supervened later. Where early excision had removed the breeding ground of devitalised tissues on which bacteria could multiply, gas gangrene and the more calamitous manifestations of sepsis were seldom seen; but once infection had appeared rapid disinfection proved impossible, and it was clear that any attempt to remove bacteria already established, mechanically by excision, or chemically by strong antiseptics, did more harm than good. Three methods proved their worth in such cases. In the French army the combination of free drainage, abundant absorbent coverings, complete immobilisation in plaster-of-paris, and infrequent dressing, which had been advocated in the Franco-Prussian war by Ollier, once again proved phenomenally successful. At Compiègne, Carrel worked out the plan of intermittent irrigation with hypochlorite solutions. In the British army, while many followed Carrel, excellent results were obtained by the use of "lymphagogues" in the form of hypertonic solutions of common salt or magnesium sulphate. Common to all methods was the insistence on free drainage and rigid immobilisation.

During the last twenty years surgery has been in the hands of men trained in the war, and the lessons of the casualty clearing station have dominated technique. Gentle surgery, though it is often attributed to the example of men like Lane, Halsted and Moynihan, is above all an acknowledgment of the basic truth that clean repair is the work of healthy tissues, a truth rediscovered in the tragic school of war. Relying on rigid care to exclude bacteria, and on the bactericidal power of the tissues to kill the few stray intruders, the modern surgeon has little use for antiseptics in planned operations and little need for them afterwards. Anatomical approach, clean cutting, careful hæmostasis, gentle retraction, reconstitution at the end of the operation of each divided plane with the obliteration of every dead space, and the use throughout of ligature and suture material of the finest calibre compatible with strength, ensure consistent healing by symptomless first intention—a different matter from union with some reddening of the skin edges and a little discharge between the sutures that passed for first intention in the early Listerian period, and that was first intention in comparison to the gross suppuration that preceded it.

THREE POST-WAR DEVELOPMENTS

In considering the present attitude towards contaminated or infected wounds, three developments of the post-war period must be taken into account. The first is the continued advance of bacteriology, and the appreciation by surgeons that of the bacterial cosmos the great majority are harmless or even useful fellow citizens, while of those that are pathogenic the majority are unlikely to establish themselves in wounds unless they are introduced in great numbers or meet with a diminished local or general resistance. Streptococci alone are dangerous in minimal quantities, and they alone can establish themselves among the healthy tissues of a healthy victim. The chief danger at an operation where the dressings and instruments have been properly sterilised is by droplet infection from some member of the team or a spectator who harbours a streptococcus in his pharynx.

The second is the invention of the sulphanilamide group of drugs. Before and during the war a number of antiseptics more effective and less toxic than the old ones had been found, but the perfect substance, one lethal to bacteria but harmless to the host, seemed to elude discovery. Ehrlich's salvarsan had shown that such selective action was possible, but the hopes that it raised were deferred when it became apparent that the arsenical compounds acted on the spirochæte family only. Sulphanilamide, introduced by Domagk in 1935, has shown that the ideal is not a dream. Neither this drug nor any of its therapeutically active chemical relations is entirely innocuous, though some such compound may yet be evolved; but their power to damage the streptococcus and other organisms is quite out of proportion to their mild and inconstant toxic action on the tissues of the host. The rapid subsidence of acute infections of the hand contracted at operation of post-mortems, even without drainage, and the cure of cases of meningococcal and streptococcal meningitis, have shown how potent these substances are to save lives that were forfeit.

The third development is the popularisation and intensive study of the French army method of no dressings and prolonged immobilisation in the treatment of established infections. The method was extended during the post-war period to the treatment of osteomyelitis by Winnett Orr, and was found during the Spanish war to be the best method of treating the wounded, especially the civilian casualties from air-raids.

QUESTIONS STILL TO ANSWER

Now, after twenty years of quiet advance and leisurely study of wound treatment and wound healing in planned and curative surgery, the problem of lacerated and contaminated wounds is with us again, and with us in an even more serious form, for the injuries of the victims in an air-raid seem to be on

the average worse than those of the wounded from a battlefield in the last war. We are back to the old controversy on the relative merits of healing by first and second intention and to the realisation that pus may be laudable.

We know how to deal with the clean wounds we make. We learned much of the treatment of lacerated and contaminated wounds in the last war, and at the end obtained results incomparably better than at the beginning. How far will that knowledge help us today, and how far will it be modified by the advances that have been made in the laboratory, by the experience of the Spanish war, by what is even now being learned in our units? Where should the primary surgical treatment of the wounded be carried out? What treatment should they receive before this, and by whom? Should we excise all wounds, or only those grossly lacerated and contaminated? After excision, should we suture them, or drain them and leave them open; are we right to attempt primary union, or should we choose second intention healing with its increased safety? If we suture, how can we guard against secondary infection later? What type of dressing should we use, and when, where and by whom should it be changed? When we dress excised wounds should we wear gloves and masks, and use the same precautions as at operation? How should we use antiseptics, and which are best; should we combine them with the first dressing, apply them to the wound in combination with excision, reserve them for cases already infected, or avoid them as far as possible? What is the place of active and passive immunisation in the prevention of infection and of specific antisera and vaccines in its treatment? What will be our attitude to chemotherapy? Should we give it in prophylaxis or limit its use to cases with evidence of infection? Can we administer these drugs safely to men who are already suffering from shock and loss of blood, and how long can we continue them without risk? Will they protect our wounded from secondary infection, allowing us to undertake primary suture more often and to dispense with some of the more irksome precautions afterwards? If we decide against primary suture in a particular case, are we committed to the method of plaster and no dressings? Is plaster-of-paris necessarily the best way to immobilise a gunshot fracture, and does a drained wound progress better when the dressings are left unchanged than when it is treated by intermittent irrigation or by hypertonic packs?

Such questions arise today, and they can be answered only by test and trial. The problem is in truth simple enough. It is a fight between germs (to use an old word which has the great merit of comprehensiveness) on the one hand and the patient on the other. Watching this fight, like Pallas Athenæ poised above the combat between Hector and Achilles, stands the surgeon. He is free to help the one and hinder the other by every means in his power, and is not restrained by rules of warfare, moral scruples or fear of retaliation from using any mechanical, chemical or biological weapon that he can devise. But while he may take what steps he chooses, he must first study his ally, his enemy and his weapons, and he would do well to remember Hunter's warning against "the conceit of surgeons who think themselves possessed of power superior to nature." Particularly should he avoid the specious argument "nothing is happening, therefore I must do something." In nature, whether we consider the animal or vegetable kingdom, the structure of human society or the strata of geology, stability as we see it is not inertia but the nice balance of many forces that have come by mutual interplay over ages to a state of equilibrium. Every action of man which disturbs that balance lets loose these opposing and cancelled forces, and sets in motion a train of events which is usually unforeseen and may be disastrous.

SPECIAL ARTICLES

VIRUSES

TILL the end of last century the word virus was used to denote infectious agents without regard to their nature. The observations of Iwanowski in 1892, confirmed by Beijerinck in 1898, that the juices of mosaic-diseased plants were still infectious after passing through Chamberland filters, resulted in the word being applied only to those infectious agents capable of passing through filters that retain ordinary bacteria. Since this original discovery a mass of knowledge has been gained, and today several hundred viruses are recognised which attack bacteria, plants, insects, fish, amphibia, birds and mammals, including man; and new viruses are still being discovered. The field covered has become too vast for most medical men to keep abreast of in its entirety, but in two recent articles Stanley (1939a and b) has succeeded in summarising most of our present knowledge, as well as making some stimulating speculations for future work.

THEIR GENERAL PROPERTIES

Viruses possess some general properties in common. They reproduce only within certain living cells, and during this reproduction they may change or mutate or be caused to change or mutate, either spontaneously or as a result of environmental changes. The infected cells commonly contain inclusion bodies. Some, but not all, of the virus diseases are followed by a lasting immunity in recovered hosts. Some of the viruses withstand the action of 50 per cent. glycerin better than the majority of bacteria and many are resistant to the action of carbolic acid and other chemical agents. Another significant property is their lack of response, with few exceptions, to chemotherapy.

It is now generally accepted that living cells, and in some cases only one type of cell, are necessary for the cultivation of viruses. This may be carried out either in vivo in a susceptible host, as on the chorio-allantoic membrane of the developing chick, or in many cases in vitro in tissue-culture preparations in various types of flasks. Optimal cultural conditions vary with different viruses. Some have the ability to grow under widely varied conditions, while others require more rigidly controlled environments. Investigators are not in agreement as to the state of cells most favourable to the propagation of viruses. Parker (1938) maintained that functional activity is desirable. Zinsser and Schoenbach (1937) found that growth of the virus of equine encephalomyelitis went on as long as cellular respiration increased, but that the rickettsia of typhus multiplied as cellular respiration decreased. This latter finding has been one of the differentiating points between the rickettsias and viruses. The virus of vaccinia has been propagated in vitro when the cells were viable but not proliferating (Rivers, Haagen and Muckenfuss 1929) as well as in the presence of living actively proliferating cells. In fact, the growth of vaccinia has been carried out in the simplest of in-vitro preparations—living cells (chicken embryo) and a balanced salt solution (Tyrode's solution)—by Li and Rivers

(1930). Eagles and McClean (1931) and Eagles (1935) reported the survival and multiplication of vaccinia in a medium apparently free from whole living cells, but Rivers and Ward (1933) were unable to confirm this finding. Attempts by MacCallum (1936) to grow the virus of psittacosis in a cell-free medium were also unsuccessful.

The manner in which viruses multiply remains a subject for conjecture. In the case of phage, Northrop (1938) considers that multiplication may be more simply explained by analogy with the autocatalytic formation of pepsin and trypsin than with the far more complicated system of living organisms. Krueger and Fong (1937) have shown evidence for the existence of an inactive precursor or pro-phage. However, no evidence has been obtained for the existence of inactive precursors having chemical properties similar to those of the viruses and a multiplicity of precursors must be postulated, since a given host cell is capable of producing any one of hundreds of different viruses or virus strains.

Many of the cells infected with a virus contain inclusion bodies in their nucleus or cytoplasm or both. In certain diseases—e.g., fowl-pox, vaccinia and psittacosis—these cytoplasmic inclusion bodies consist of or contain smaller bodies, the so-called elementary bodies, which have the properties of the viruses. In other diseases, such as rabies and yellow fever, the status of the inclusion body is unknown. The picture is complicated by the production of cell inclusions by processes other than the virus diseases. Belt (1939) has found inclusions in the liver cells of patients dying from burns, similar to those found in the liver in yellow fever. Olitsky and Harford (1937, 1938) were able to produce inclusions in guineapig tissues by the injection of aluminium hydroxide, ferric hydroxide, carbon, and normal brain tissue. The production of inclusions by non-infectious agents tends to lessen the importance of cell inclusions as a point of diagnosis of a virus disease.

In the majority of animal virus diseases recovery is accompanied by life-long immunity, as in yellow fever, but it may be of only a few weeks duration, as in herpes simplex, influenza and the common cold. It is probable that the mechanism of virus immunity varies in different diseases. In some there are virucidal immune bodies in the blood, in others the immunity appears to be in the tissue cells, and in many of these the immunity is probably due to persistence of the live virus in the cells, as has been demonstrated by Bedson (1938) in psittacosis. In the early days of virus study it was generally believed that infection was essential if active immunity to a virus was to be established. It has since been shown that the viruses of foot and mouth disease, herpes, distemper, psittacosis, equine encephalomyelitis, influenza, yellow fever, Rift valley fever, rabies, and lymphocytic choriomeningitis can immunise when injected in sufficient amounts in the dead state.

During their growth for long periods in tissue culture certain viruses—e.g., yellow fever—have become sufficiently attenuated to be injected in the living state without producing severe reactions. The growth of vaccinia in tissue-culture flasks and on the chorio-allantoic membrane has provided a bacteria-free source of virus for jennerian prophylaxis which may one day supplant calf lymph. For many years influenza has been one of the chief causes of loss of time from work as well as loss of life and only symptomatic treatment has been available. It is possible that the growth of the virus of epidemic influenza in tissue culture may provide a more satisfactory weapon for preventing and treating this disease.

THEIR NATURE

Until recent years viruses were regarded variously as invisible forms of ordinary bacteria, as protozoa, as some new type of invisible living organism, as enzymes, as unusual products of cellular metabolism, as toxins, or as different kinds of chemical principles. With the exception of certain viruses of the elementary-body type, such as vaccinia, attempts to isolate a virus in tangible form had failed. However, in 1935, Stanley isolated from mosaic diseased plants, by chemical means, a material which appeared to be a protein of high molecular weight and which was distinguished by the fact that it possessed the properties of the tobacco mosaic virus. This was confirmed and followed by the isolation, by the same or similar chemical methods or by means of differential centrifugation, of over twenty similar substances of high molecular weight possessing some of the properties of the viruses or virus strains. Bawden and Pirie (1937a and b, 1938) have isolated heavy proteins, certain of them crystals, which act in the same way as the virus from enation mosaic, cucumber mosaic 3 and 4, potato Y and bushy stunt of tomato. Stanley and Wyckoff (1937, 1938) have found the activity of the virus was associated with a heavy protein in tobacco ringspot, severe etch, cucumber mosaic 1 and latent mosaic viruses. Beard and Wyckoff (1937) isolated the Shope papilloma virus, Wyckoff (1937) the equine encephalomyelitis virus, Schlesinger (1933) a coli-bacteriophage, Northrop (1936) a staphylococcus bacteriophage, Claude (1938) the Rous sarcoma virus and Pirie, Smith, Spooner and McClement (1938) the tobacco necrosis virus as materials of high molecular weight.

All viruses so far isolated appear to have a high molecular or particle weight, yet this fact alone cannot be used as a criterion of virus activity, for some of the virus nucleo-proteins may be inactivated by appropriate treatment without changing their size greatly. However, no entity having a size smaller than that corresponding to a molecular weight of about 400,000 has been found to possess virus activity, and hence it is probable that a certain amount of structure may be necessary to support such biological activity.

In every instance the preparations have not only possessed virus activity but have had an activity much greater than that of the starting material. Stanley does not think one is justified in assuming that the maximum concentration has been achieved in every instance, that is to say that the different preparations are essentially homogeneous and hence represent the different viruses in an essentially pure condition. But he does believe that the results available from work on tobacco mosaic virus preparations justify the conclusion that they are homogeneous and hence actually consist of virus alone. The material which has been isolated from mosaic diseased plants has been found, with few exceptions, to have definite and constant chemical, biological, immunological and physical properties. Data indicate that it is a conjugated protein containing 95 per cent. protein, 5 per cent. nucleic acid and no lipoid. It has been found to yield only amino and nucleic acids on hydrolysis. The nucleo-protein contains 50 per cent. carbon, 7 per cent. hydrogen, 16 per cent. nitrogen, 0·25 per cent. sulphur and 0·6 per cent. phosphorus. The material gives specific precipitin and anaphylaxis reactions and when highly purified it is impossible to detect the presence of extraneous substances by immunological tests.

Of great significance are the findings that treatment which has caused changes in one or more of the chemical or physical properties of the material has also caused a change in virus activity. Digestion with

certain enzymes or denaturation by acid, alkali or heat, dodecyl sulphate or urea causes loss of activity, and in general the rate of denaturation or digestion and the rate of loss of activity have run parallel with one other.

It appears that with varying degrees of certainty a great variety of viruses have been obtained in an essentially pure form. Some of these viruses affect plants, whereas others affect animals. Stanley believes that virus activity, whether it is manifested in plants or animals, is manifestly the same. Some of the viruses are conjugated proteins containing 5 per cent. nucleic acid, others contain about 40 per cent. nucleic acid, others contain nucleo-protein plus additional carbohydrate, and still others these last two plus some lipoid. McFarlane, MacFarlane, Amies and Eagles (1939) found that vaccinia virus contains lipoid as well as protein, carbohydrate and nucleic acid. As a result of their critical examination they conclude that, while the virus of vaccinia is more complex chemically than the plant viruses, there are no grounds for believing that its structural integrity depends on any fundamentally different physical principle. The sizes of the purified viruses have been found to correspond closely to the sizes previously estimated by Elford and others from filtration data on impurified or semi-purified preparations. As a result of the purification studies, it has been found that viruses differ tremendously in shape. Tobacco mosaic virus, its strains and related viruses, and latent mosaic of potato virus are long thin rods, whereas tobacco ringspot and Shope papilloma viruses appear to be spherical.

Because of the indication that viruses are protein or protein-like in nature, there has been a tendency to assume that they are non-living and are merely ordinary protein molecules like egg albumin. The question whether viruses are living or non-living in itself seems to be of little importance, for the word "life" is merely a definition of degree. However, intensive study of the nature and mode of action of viruses may yield knowledge on the problems of normal and abnormal metabolism and on the nature of life.

The chemist, taking the properties of the purified viruses so far isolated as his guide, has little or no difficulty in coming to the conclusion that they are protein molecules. Pathologists and biologists in general have, on the other hand, considered at any rate the larger viruses to be living organisms. Rivers (1938) has suggested that the larger viruses may be living organisms, the middle-sized viruses representatives of an unknown form of life, and the smaller viruses non-living agents, but that one group probably shades off into the next. Green (1935) and others have suggested that viruses are simplified fragments of living protoplasm arising from organisms by a process of retrograde evolution under parasitism, involving loss of function and associated substance, and that this process may result in forms ranging from a single colloidal molecule to entities almost indistinguishable from ordinary living organisms.

In recent years variations of many viruses have been found occurring both naturally and as a result of artificial production. Findlay (1939) could find no essential difference and certainly no clear dividing line between the types of variation encountered in multicellular and unicellular organisms on the one hand and animal and plant viruses on the other, despite the fact that neither in bacteria nor in viruses is there clear evidence that hereditary characteristics are transmitted by structures of the type of chromosomes or genes. He concludes that although variation may not be an exclusive property of living organisms, or even of organic compounds, the close analogy between the variations found in animal viruses and those in animals and plants makes the adoption of a vitalistic conception of the nature of animal viruses almost inevitable.

The ability of organisms to reproduce is associated with nuclear material and it is assumed that the basic unit of this material is a gene, perhaps a single nucleo-protein molecule. Further, all viruses appear to be, or at least contain, nucleo-proteins. From this Stanley concludes that the properties of the viruses composed of nucleo-proteins are essentially the properties of a gene or a group of genes were they capable of an independent existence. He suggests that the characteristic structure which permits a virus to enter into the metabolic chain of events within cells may have a direct bearing on the advent of cancerous growths.

Stanley believes that there is in reality a continuum from simple to complex structures, from molecules to organisms, and that after all there is no great difference between the two. If this is so we must look for further elucidation of the nature of viruses in structural organic chemistry.

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The Lancet 100 Years Ago

March 28, 1840, *p.* 17.

From an article by Mr. Wm. Erasmus Wilson.

The use of the bath is a measure of the utmost importance to the preservation of health, one of easy attainment by all classes of society, but one which the perversity of human nature leads us to despise, from its very facility of acquisition. In large cities, where habitations are crowded together, streets are ill ventilated, and the atmosphere is impregnated with soot, dust, and animal exhalations, the bath is absolutely necessary to health, and if more frequently employed would certainly preserve its votaries from many painful and distressing diseases. To the affluent the bath-room is the abode of luxury, but the humblest may attain every necessary object by sponging the skin over every part of its surface with common water, and once in the seven days with a weak solution of subcarbonate of soda. By such simple means the sentient nerves would be healthfully stimulated, the capillary system of the skin excited to perform its natural offices, and disease, particularly of the cutaneous kind, effectually averted.

THE R.G.'S HUNDREDTH REPORT

BETWEEN July 1, 1837 and June 30, 1838 the first annual report of the Registrar-General of England and Wales records that 132,437 deaths took place in the first five years of life, 15,604 in the second quinquennium and 8776 in the third, a total loss of nearly 157,000 children before the age of 15. If the population at this date had experienced the death rates of 1937, to which year the 100th report of the Registrar-General relates,[1] the number of deaths would have been 33,407 at 0–5, 3,375 at 5–10 and 1,937 at 10–15, a total loss of 38,719 lives before age 15, or rather less than one-quarter of the actual loss. Again, of each 100 male and female babies aged 1–2 in 1837 it is estimated that approximately 71 of each sex survived to age 35 and that 36 males and 41 females survived to age 65. At the death-rates of 1937 the numbers of survivors would be 91 males and 92 females at age 35, 60 males and 69 females at age 65. So far have we come on the road to saving child life.

1837 AND 1937

It is not easy to compare the relative frequency of causes of death in 1837 and 1937 owing to changes in nomenclature and classification, but in some approximate comparisons the Registrar-General reaches the following results. In July to December 1837 there were 7,252 deaths from measles and scarlet fever; in the same period of 1937 and in a population of the same size there were 255. On the same basis, in 1837 there were 3,044 deaths from whooping-cough; in 1937 there were 209. Smallpox accounted for 5,811 deaths in the latter half of 1837, for none in 1937. On the other hand violence was responsible for 4,845 deaths at all ages in the last six months of 1837 and at the 1937 rate there would still have been 4,206. Much of the improvement in the mortality-rates in early childhood is, of course, of quite recent date. In the years immediately preceding the Great War, 1911–14, the infant-mortality rate was 118 per 1000; in 1937 it was 61, or approximately half. Still more dramatic is the decline at ages 1–5, for the rates per 1000 were nearly 16 in 1911–14, 9 in 1921–30 and only 5 in 1937.

Such is the brighter side of the picture. On the other hand, in a special study of mortality under two years of age in various countries the Registrar-General shows that the position in England and Wales still leaves much scope for improvement. For instance, in 1935–36 the infant-mortality rates of Norway, Holland and Sweden were 25–30 per cent. below that of this country, and whereas only 36 out of each 1000 children born alive in New Zealand and about 50 in Australia, Holland and Norway failed to survive to their second birthday, the corresponding number in England and Wales was 74. Within the country large differences are also apparent. In the county boroughs the stillbirth-rate in 1933–37 was only 3 per cent. above the corresponding rate in the rural districts, and in the first week of life the excess was still only 4 per cent. But from 3 months of age to the end of the first year the rate in the large towns was no less than 75 per cent. above the rate in the rural districts. In the same years the rate of infant mortality at 3–12 months was 9·8 deaths per 1000 live births in Oxford, Canterbury and Ipswich (aggregate), while in Birmingham it was 22, in Manchester 26, in Wigan 33 and in Liverpool 37.

1. The Registrar-General's Statistical Review of England and Wales for the year 1937. New Annual Series No. 17. Text 231 pp. H.M. Stat. Off. 1940. 3s. 6d.

TOWN AND COUNTRY

The Registrar-General again emphasises the inevitable conclusion that a very considerable further reduction in the infant mortality of some of our towns is practicable. Corresponding differences are apparent at ages 1–5. In the county boroughs the death-rates from diphtheria and whooping cough are about twice those in the rural districts, from measles three times as high, and from pneumonia and bronchitis about 50 per cent. in excess. Of the principal causes of death at these ages only tuberculosis and violence show little difference between the town and country environment. At ages 5–10 diphtheria is by far the most important cause of death and at 10–15 it ranked third in 1937. It may well be asked, in the Registrar-General's words, why, if it can be virtually eliminated by preventive inoculation of the child population on a large enough scale, these deaths and the suffering endured by the 60,000 children annually notified as ill with diphtheria continue to be tolerated by public opinion.

The R.G.'s 100th report, no less than its predecessors in an honourable line, provides the public health worker and sanitary reformer with a mine of information and points the way to still further advances in national health.

MEDICINE AND THE LAW

Disputed Paternity

THE law has seldom tied itself into worse knots than in its rules respecting the proof of paternity. By last week's ruling in R. *v.* Carmichael the Court of Criminal Appeal tightens the tangle. The good old rule, enunciated in the writings of Sir Edward Coke, established a presumption of legitimacy; if the husband were within the four seas during the period in which the child must have been begotten, the courts would not listen to any evidence to prove non-access. The rule about the four seas has suffered change in subsequent centuries, but it remains the law that neither the mother of the child nor the husband is allowed to be a witness to testify to the fact of access or non-access. Decency seals their lips; they cannot give direct evidence to bastardise their offspring born in wedlock. The House of Lords by a majority upheld this principle in Russell *v.* Russell in 1924. It applies to divorce proceedings and other proceedings instituted in consequence of alleged adultery. Husband and wife can adduce evidence from other sources but cannot give the evidence themselves. We thus reach the ridiculous position that, as Lord Sumner pointed out in his minority opinion in the Russell case, the courts are debarred from hearing the testimony of those witnesses who have far the best testimony to give on the point at issue.

The principle having thus been established by the House of Lords, the divorce court began to seek a way round its manifest inconvenience. It was contended, for instance, that, if husband and wife were separated by a decree of the court, the presumption of access would be rebutted and evidence of non-access could properly be received from either of the two. The next stage was to extend this argument to cases where husband and wife were living apart under a formal separation deed. Finally Mr. Justice Langton extended it, in Ettenfield *v.* Ettenfield, to a case where husband and wife were living apart under a mere informal agreement. The wife had given birth to a child; the husband relied upon the fact as evidence of adultery and was allowed by the judge to swear that he had not had access to his wife at the material

time; the wife was allowed to give contradictory evidence as to access. The judge believed the husband and granted him a decree. The Court of Appeal, however, pulled up the divorce court in the flight from the decision in the Russell case. It declared that the husband and wife could never give evidence themselves as to access or non-access where a child had been born in wedlock, no matter whether they were living apart under a decree of the court, or under a separation deed or a voluntary arrangement.

Now comes the fresh complication in the appeal in R. *v.* Carmichael last week. Carmichael was married in 1912. His wife went away to Cambridge in August, 1914, and associated with a man named West, her husband being seldom with her. On May 18, 1915, a girl named Sonia was born. Mrs. Carmichael told her husband that the girl was not his child. In 1916 he divorced his wife on the ground of her adultery with West. In 1933 Carmichael lived in lodgings with the girl Sonia, not as father and daughter, but as husband and wife. She bore him four children. He was convicted last March of incest. He had sought to give evidence at the trial to prove that Sonia was not his daughter. He wanted to say that Sonia's mother had told him that he was not the father of the girl; he wanted to say that he believed her statement. The judge, feeling himself bound by the Russell case, refused to let him give this evidence; the rule prevented husband or wife from giving evidence of non-intercourse after marriage to bastardise a child born in wedlock. The Court of Criminal Appeal upset Carmichael's conviction. He had been deprived of the chance to give evidence of his belief that the girl Sonia was not his daughter; this was a negation of justice; it was the elementary right of an accused person to be allowed to declare his innocence. He had been permitted to deny on oath that he knew Sonia to be his daughter and yet had been precluded from giving his reasons for that denial; the Crown, moreover, had been precluded from cross-examining him about those reasons and about his alleged belief. The rule in the Russell case has thus been attacked from another side. The House of Lords will presently have an opportunity to reconsider the position. The law can hardly be left in its present uncertainty.

Surgeon's Successful Claim for Fees

A recent claim for £200 by a surgeon in the Wrexham county court brought out two facts which made the case worth reporting in the lay press. The first was that the patient (who was 67 years old) had observed, on receiving the bill for this amount, that it would be cheaper for him to die. The second was that the county-court judge, in allowing the surgeon's claim, remarked that provincial doctors were just as skilful as those in Harley Street.

The case was one in which Mr. R. D. Aiyar of Wrexham had performed two operations for Mr. W. F. Humphreys, a builder and contractor, who suffered from sinus trouble. Mr. Aiyar had given treatment before and after the operations and had been consulted over a period of seven months. He was fully prepared to justify the details of his charges. He claimed that for the second operation, which needed all the skill and technique of a specialist in ear, nose and throat surgery, a fee of 100 guineas would be entirely proper. The patient offered 100 guineas in settlement of the whole bill. The offer was not accepted. Judge Sir Thomas Artemus Jones awarded Mr. Aiyar the full sum claimed. The charges of a skilled surgeon, he said, were not based on a fixed scale like the charges of a solicitor; successful surgery was a matter of human judgment and no two cases were alike. What the learned judge said evidently needed saying. There is no reason why a well-to-do patient should expect to get surgical treatment at what may be called "cut prices" in London or elsewhere.

IRELAND

(FROM OUR OWN CORRESPONDENT)

ST. LAURENCE O'TOOLE HOSPITAL

THE scheme of hospitalisation for Dublin, as approved by the Minister for Local Government and Public Health some two years ago, provided for the establishment of four general hospitals, each with 500–600 beds, two on the north side of the city and two on the south. Three of these hospitals were to be obtained by the development of three existing hospitals—the House of Industry Hospitals (Richmond, Whitworth and Hardwicke), the Mater Misericordiæ Hospital, and St. Vincent's Hospital. The fourth was to be formed by the amalgamation of a group of three smaller hospitals—Mercer's, Sir Patrick Dun's, and the Royal City of Dublin. This scheme was approved in the spring of 1938; since then there had been apparently little progress toward its realisation, but activity was no doubt proceeding in private. The public criticism aroused by the seeming inertia irritated the Department of Local Government and Public Health, and a few weeks ago it threatened to abandon the scheme and to establish one large municipal hospital. This threat, though not taken over-seriously, caused some anxiety to those who recognised that the whole voluntary system was at stake, and that government departments are not always wise. These fears have now been set at rest by the introduction in the Dáil last week of a bill for the establishment of a new hospital to be called the St. Laurence O'Toole Hospital in or near Dublin in place of the existing House of Industry Hospitals. It is recognised that by this step the Government has definitely committed itself to the scheme of development which it had threatened to abandon. The time is, no doubt, hardly opportune for beginning large building operations, but it is the declared policy of the Government to encourage building for the sake of relieving unemployment, and it may be taken that when the present bill becomes law every attempt will be made to hasten the provision of the new hospitals. Legislation will also be required to deal with the amalgamation of the three smaller hospitals, and it is understood that agreement has been reached in a draft bill between the Minister and the hospitals concerned.

Most people assumed that the hospital to replace the House of Industry Hospitals would occupy the present site, but the department has pressed the governors of the hospital to move to a fresh site on the extreme edge of the city, 5 miles from any of the medical schools, and the governors have unwillingly agreed.

HOSPITAL BED BUREAU

It is now some three or four years since the Minister for Local Government and Public Health invited representatives of the general hospitals of Dublin which were to be specially developed to assist him in planning a hospital bed bureau. After rather tedious consideration a scheme was agreed upon. The hospital representatives pointed out, however, that until there was a substantial increase in the number of hospital beds in Dublin the bureau could hardly function with success, and the Minister was convinced

by the reasons they put forward. The plan, therefore, went "into cold storage." In recent months, however, a public agitation has sprung up for the immediate establishment of a bed bureau, and both the Minister and the hospital authorities have been the subject of severe, though generally ill-informed, criticism for delay. The Minister has decided, therefore, to proceed with the plans for the bureau, and has now introduced a bill in the Dáil to authorise its establishment. The text of the bill has not been made public at the time of writing. With the present shortage of beds the bureau may be called upon to function in vacuo.

SCOTLAND

(FROM OUR OWN CORRESPONDENT)

JOINT HOSPITAL SCHEME FOR STIRLINGSHIRE

AN inter-hospital committee was formed more than a year ago to consider the organisation of the Stirling, Falkirk and Alloa areas as a hospital unit. Now the medical staffs of the three hospitals have formed a committee and consultation has already been held with the chief medical officer of the Department of Health about the staffing of the hospitals in this area. It was decided that in any emergency Stirling, Alloa and Falkirk and another hospital which is being built at Larbert shall pool their resources as regards personnel and mutually assist each other. Obstacles have been found in the way of such coöperation in the past because of prejudice or perhaps short-sighted parochialism, or the faculty of working into grooves, but war has swept all obstacles away. The medical superintendent of Stirling Royal Infirmary urges that when peace comes it must be insured that this coöperation continues. The way to achieve this is to establish a joint contributory scheme for the whole district, common to the three hospitals, and to try as far as possible to have a team of specialists living in the district who can give the benefit of their skill to any of the hospitals as needed.

PARATYPHOID IN GLASGOW

There has been a moderately severe outbreak of paratyphoid fever in the Glasgow district, the number of cases now reported being over 190 with 3 deaths. The three fatal cases were all men, 2 in Glasgow and 1 outside the city. There has been a popular feeling that the outbreak is in some way associated with the passage of the new liner, the *Queen Elizabeth*, down the Clyde. It happens that a similar epidemic broke out in the city four years ago when the *Queen Mary* made her first journey down the Clyde. The deputy medical officer of health for Glasgow describes this fact as sheer coincidence, and says there is no ground for the belief that these big liners stir up a mysterious germ from the river bed. A number of cases have been reported from the riverside district, but there have been equally big numbers from other districts and no single area can be plotted as the centre of the outbreak. There is no indication that the epidemic is becoming more serious.

HOSPITAL SUPPLIES FOR ORKNEY

The Scottish branch of the British Red Cross Society have dispatched large supplies of hospital dressings, garments and furnishings to the Orkney Islands, the first place in the British Isles to suffer civilian casualties from an air-raid. The material has been sent to the Balfour hospital and to hospital huts established by Toc H. The Red Cross have promised further supplies and have also decided to present six light ambulances to the military authorities there. Until a short time ago the Scottish Red Cross had no branches in the Orkney or Shetland Islands, but branches are now being opened.

UNITED STATES OF AMERICA

(FROM OUR OWN CORRESPONDENT)

RIVAL HEALTH POLICIES

THE Committee of Physicians for the Improvement of Medical Care held its annual meeting at New Haven on January 20 and elected officers. The new chairman is Dr. Borden S. Veeder of St. Louis, Mo. and the vice-chairmen Dr. Hugh Cabot of Boston, Mass. and Dr. Milton C. Winternitz of New Haven, Conn. Four new members were elected to the committee from New York where the support for this group is unusually strong. Statements were authorised regarding the "platform" recently formulated by the board of trustees of the American Medical Association [1] and the National Physicians Committee. These have been circulated among the signatories of the committee and largely reproduced in the lay press. The committee indicates several similarities between the present platform of the A.M.A. and the "principles and proposals" which it formulated in 1937. However, it is critical of some ambiguities and some implications in the official platform.

For example in proposal 7 the A.M.A. advocates the continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

The committee agrees that the maintenance of high ethical standards, of personal relations between patients and physicians, and of personal responsibility of physicians to patients are highly desirable. However, if the clause aims to proscribe group medical practice or payment for medical services by any other system than that of fee-for-service, it can only impede the development it professes to promote. The committee is aware of no evidence that payment by the government through salaries is more deleterious to character or efficiency than payment by the same agency of fees-for-service. On the contrary, there is much evidence to prove that when payment for medical care is made to the physician for the patient by any third party, fees-for-service are more conducive of evils than either salaries or remuneration on the capitation principle. In any case it is not the prerogative of the federal government to dictate terms of medical practice to the states. This would be peculiarly at variance with the principles of local autonomy enunciated in American Medical Association proposals 4 and 5.

The last "plank" in the A.M.A. platform is, in the committee's opinion, obviously concerned with health insurance because although this ominous phrase does not appear in proposal 8, the official comment on that proposal reads :—

Careful study of the history of the development of medical care in various nations of the world leans to the inevitable conclusion that the introduction of methods such as compulsory sickness insurance, state medicine and similar technics results in a trend toward communism or totalitarianism and away from democracy as the established form of government.

The committee rejoins that it is not aware of any evidence that will support this statement. From the first they have affirmed that the problem of medical care cannot be solved by health insurance alone, but they feel that it is a mistake to exclude from con-

1. *J. Amer. med. Ass.* 1939, **113**, 1966.

sideration a method which has been so extensively employed. The committee goes on to say :—

The most satisfactory formulæ are likely to be found by experimentation, well conducted. Methods of finance are quite as valid fields of inquiry as methods of therapy or prophylactic procedures. The real road to totalitarianism lies in the arbitrary limitation of the attempts of the people to improve their condition by peaceful methods consistent with the philosophy of democratic government. Nothing could be more contrary to the spirit of a federal democratic union than the enactment of a federal health bill that excluded from its benefits that state which adopted a particular procedure to finance its program or which included in its program groups of the population above some arbitrary level of income. However, only by the incorporation of such provisions could a federal health bill prevent the introduction of compulsory health insurance by the states.

The committee regrets that the platform of the A.M.A. includes no clause urging that provision be made for the support and expansion of medical education and research. "Without such provisions," they add, "the chief aim of any sound program, continuous improvement of medical care, cannot be realised."

The profession in this country has been widely circularised for funds to support a "National Physicians Committee." The Committee of Physicians, responding to requests for information from many of its signatories, draws attention to editorials in *Minnesota Medicine* (December, 1939, p. 842) and the *Journal of the Connecticut State Medical Society* (December, 1939, p. 685). From these it concludes that the new national committee is merely a lobbying organisation designed to promote the official programme of the A.M.A. without subjecting its income to the tax which lobbying interests must pay in this country.

COLD THERAPY

A preliminary report on the use of crymotherapy in the Lenox Hill Hospital was made to the New York Academy of Medicine on Feb. 20. Twenty-seven patients have received treatments to a total of 2856 hours, the maximum treatment received by any one patient being 330 hours in a period of 106 days. It has been found possible to reduce a patient's temperature 10–18° F. below normal and to maintain this depressed temperature for periods ranging from a few hours up to three days. No conclusions are drawn as to the value of the treatment, but temporary relief from pain has been experienced and on its return the pain is often found to be less severe than before treatment.

IN ENGLAND NOW

A running commentary from our Peripatetic Correspondents

SEDGEMOOR was the last battle fought on English soil and long may it remain so. In the Bridgwater museum there is an excellent plan of the battle, but, perhaps more interesting to one entitled to wear the same old school-tie as Judge Jeffreys—a somewhat dubious privilege—is the tavern receipt given to him at Tunbridge Wells, where he spent a month taking the waters before setting out on the Bloody Assize. It seems that he took other things there besides the waters, for the receipt shows an item of £2 10*s.* 2*d.* "for 86 gallons of strong beers"—pretty good going for one man in a month, though the possibility of friendly helpers cannot be excluded. From this receipt it may also be inferred that Jeffreys was a cleanly man since he paid nine shillings "for heating ye oven 9 times," presumably for bath water; and that he was a chilly mortal since he paid two guineas for "3 loads and ½ of wood," six shillings "for billett ffagotts" and four shillings for "4 bushell of coles." His lodgings cost him £5 a week and his total bill for the month, which included some £25 for care of coach and saddle horses, amounted to £50 12*s.* To his credit be it recorded that he paid it, and apparently without demur.

* * *

There can seldom have been a time when the surgical profession was more urgently called upon to exercise our national gift of improvisation, but with some honourable exceptions the response has been poor. The younger generation of surgeons are, not unnaturally, inclined to think that the glitter of rustless steel and chromium plate is a necessary accompaniment to operating. Few realise that surgery, and even successful surgery, can be executed with a fish-kettle, a deal table and carbolised towels, and that anæsthetics can be given with a towel, a safety-pin and a bottle of ether or even chloroform, and there will in fact be few places or times when such extremes need be faced. But this is going to be a war of resources; the financial burden is going to strain the Exchequer to near breaking-point, and high authority is behind the view that too much has already been spent on A.R.P. and that further spending on provision for dealing with casualties is out of the question. The profession must get down to making the most of what is at hand. Some men quail at the difficulties but others have already faced and overcome them. It may be impossible to improvise a drainage system, but a man of the right temperament can, by diplomacy secure additional sanitation—and do many other things that are officially impossible, unheard of, unprecedented and even prohibited.

England is a self-governing country and Whitehall cannot override the Local Government Act except in cases of gross neglect of obligations. Local authorities are extremely tenacious of their rights and jealous of their prerogatives. They resent to the point of obstinacy any attempt to dictate to them an action which involves the expenditure of money to be raised from the rates, and expect Whitehall to pay for every piece of work carried out in their hospitals on account of war preparations, even when it is a substantial improvement of their property. This attitude is easily understood, but when one considers the lavish expenditure of money by county councils on their own new hospital buildings, and the standard of the accessory services they think proper to budget for, it is extraordinary that they should prove recalcitrant in accepting partial financial responsibility for additional sanitary, heating and lighting costs, where admittedly the standard to be reached is higher than the peace-time requirements absolutely demand, but not so high as their own standard for new buildings.

When it is remembered that patients resident in a London borough may now, owing to the exigencies of dispersal, pass into and through the territories of five counties, two urban district councils, and a joint board, is it any wonder that delays and fiascos are the order of the day? We must look forward to the time when one authority, constituted like that for the Port of London, controlled by Parliament but independent of politicians, is responsible for the health services

of this country. Why, why should the men and women all equally citizens though drafted into the Army, Navy, Air Force, Police or home Civil Service, or just wounded in war hazard at home, be treated separately? Why should services be triplicated or quadrupled? Why spoil all four ships for the sake of giving each its right coloured tar? Why in war-time not adopt and adapt the existing facilities for widely dispersed small fighting units, such as the Army has never had to provide for before? Why not use a dispersed organisation like the Red Cross (and its now constituent parts) for dispersed demands? Why court criticism, trivial in individual instance but cumulative to the point of scandal in sum?

* * *

Wags say that Hitler's secret weapon is hidden in Whitehall, and no wonder. This extraordinary country of ours must be utterly inexplicable to others. To do the job of looking after potential casualties, we employ two, if not three, ministries, and allow scores of administrative bodies to quarrel over the expenditure of money that must ultimately come out of the same purse. It is not the hundreds of thousands of pounds that matter, it is the smaller sums that should be spent locally, for want of which a whole organisation may fail to function, or an elaborate machinery creak and groan. Of course, here as everywhere, character tells. A medical superintendent here, a chairman of committee there, is strong enough to get things done in spite of obstruction, red tape and sheer ineptitude. In most county hospitals the medical superintendent is an autocrat, but when once an A.R.P. authority has gained or "won" possession of a part of his premises for a first-aid post the autocrat must wait humbly at the door till the portly lady commandant consents to admit him, and allows him, and a visitor, to see the preparations made for the treatment by a crowd of amateurs—under a visiting doctor of course—of the wounded, crushed, shocked or gassed. Sensible people would think it obvious and essential for an F.A.P. located *in* a hospital to be administered and staffed *by* the hospital. But no doubt we shall muddle through. If a great bombing comes there will be men strong enough to sweep aside hindrances and get on with the job.

* * *

One more thought while my visit is still fresh in mind. How does the Egyptian medical student compare with his European confrère? The hardest worker in a British school would by oriental standards be almost a slacker. Games, communal interests, social relaxations of all kinds, all the familiar features of a British student's life are not for him. This is partly a consequence of the elaborateness of his curriculum, which aims at preparing the student for duties and responsibilities which in England would not be undertaken until a specialised postgraduate training had been gone through. The Egyptian academic year is also shortened by a long summer vacation and numerous religious and official holidays. And the Egyptian student's idea of using these intermissions is to repair to his home and read solidly for nine or ten hours a day. He is constitutionally able to memorise and reproduce whole paragraphs or even pages, but there is a danger that he may never acquire a sense of the relative values of many facts even if he grasps the meaning of the words. It is not easy, therefore, for an examiner to assess with justice the practical value of such knowledge, and ever-increasing emphasis is laid upon the clinical side of the examination. Nor is one able from a comparatively short observation to judge what type of practitioner will be evolved. Sir Charles Gordon-Watson has referred in these columns to the value of our traditional clinical teaching which has produced so useful a practitioner—self-reliant because partly self-taught. He employed a simile which is admirably expressive, the old-fashioned ladder in preference to the escalator. This appeals to me strongly with the memory of the other extreme—the student who believes he can be entirely self-taught by home study, by memorising vast tracts of textbooks and rarely seeing a patient or learning to appreciate the instruction of experienced seniors. Yet there is much in the Egyptian examinees to admire and to approve. They display a solicitude not often to be found among British students to save their examiners annoyance and trouble by marking their answers, and their writing is almost invariably legible. Occasionally the spelling and composition would be creditable even from a good British representative, although there is a striking uniformity in the answers and an eccentricity of expression often betrays an obvious misapprehension. They share with our own students the familiar curse of abbreviations and this appears to come less from laziness than from a fundamental misconception that the principle is a professional convention or perhaps good form. I culled such gratuitous monstrosities as 1stly; c̄ out; black H_2O fever. It was interesting to grapple with one candidate's effort over cardiac arrhythmia and attempt to trace the sense in: "If we listen over the heart we find the same thing, and this differentiates it from extra-systoles which on listening over the heart we hear the dropped beat while in heart-block we don't hear it." But I wonder what sort of a job most of us would make of an examination in an alien tongue!

PUBLIC HEALTH

Is German Measles Notifiable?

THERE is still doubt as to whether the compulsory notification of measles includes German measles. Measles, which was made compulsorily notifiable by Statutory Rules and Orders 1940 No. 204 of the Ministry of Health under section 143 of the Public Health Act 1936, is not defined in the order, the provisional order issued in October 1939 or in the circular which accompanied the latter. Nor has the Minister made clear in any way whether or not he desires notification to extend to rubella. Some medical officers are of opinion that measles covers both morbilli and rubella, probably because in the tables of infectious disease given in the annual report of the Chief Medical Officer measles and German measles are bracketed together, and in some localities where measles has been notifiable both diseases are included. Other medical officers, in view of the trivial nature of rubella, think that the Minister could not have countenanced wasting shillings on it, and therefore did not intend it to be notified. The Oxford Dictionary defines German measles as a contagious disease distinct from measles, thereby implying that in popular parlance measles without a qualifying adjective does not cover German measles, but the Minister of Health may not think himself bound by the rulings of the Oxford Dictionary.

Cerebrospinal Fever

In the week ending March 9 there was, for the first time since the middle of last December, a fall in the notifications of cerebrospinal fever. The number of cases reported was 606 compared with a corrected

total of 617 in the previous week. Taking broad regions this fall was, however, confined to the eastern and south-eastern counties, the administrative county of Southampton being particularly prominent with 51 cases in the week-ending March 2 and only 24 in that ending March 9. In the northern, midland and south-western counties a slight rise in incidence continued, while in Wales and Monmouth the level has been practically unchanged for a month. In the first ten weeks of this year the number of notifications have reached a total of 3558 compared with 1508 in the whole of 1939 and some 3500, or practically the same number, in the *whole* of the 1915 epidemic.

Infectious Disease in England and Wales

DURING THE WEEK ENDED MARCH 9, 1940

Notifications.—The following cases of infectious disease were notified during the week: Smallpox, 0; scarlet fever, 980; whooping-cough, 519; diphtheria, 662; enteric fever, 23; measles (excluding rubella), 4888; pneumonia (primary or influenzal), 1883; puerperal pyrexia, 155; cerebrospinal fever, 606; poliomyelitis, 5; polio-encephalitis, 1; encephalitis lethargica, 8; dysentery, 42; ophthalmia neonatorum, 90. No case of cholera, plague or typhus fever was notified during the week.

To the 606 cases of cerebrospinal fever Berks contributed 16 (Reading 5), Buckingham 13 (Aylesbury 9), Chester 10, county of Derby 24 (Derby 4, Chesterfield 8), Devon 14 (Plymouth 5), Dorset 13, Essex 22 (Colchester 6), Gloucester 10, Kent 15, Lancaster 44 (Bolton and Manchester each 7, Liverpool 13), County of London 35 (Paddington, Wandsworth, and Woolwich each 4, Stepney 5), Middlesex 13, Northumberland 10 (Newcastle-on-Tyne 4), Salop 10 (Shrewsbury 4), Somerset 26 (Bath 7, Taunton 4), county of Southampton 24 (Southampton 9, Andover 4), Stafford 20 (Walsall 4), Surrey 21 (Kingston-on-Thames 4), Warwick 25 (Birmingham 15, Coventry 5), Wilts 20, county of Worcester 10 (Worcester 4), Yorks (West Riding) 39 (Bradford 8, Sheffield 11), Denbigh 17 (Wrexham U.D. 5, R.D. 9), Glamorgan 31 (Cardiff 7, Swansea 4, Port Talbot and Rhondda each 5), Monmouth 16 (Newport 10).

Deaths.—In 126 great towns, including London, there was no death from smallpox, 3 (0) from enteric fever, 2 (0) from scarlet fever, 2 (0) from measles, 7 (0) from whooping-cough, 24 (1) from diphtheria, 31 (8) from diarrhœa and enteritis under 2 years, and 429 (28) from influenza. The figures in parentheses are those for London itself.

Fatal cases of diphtheria were scattered over 18 great towns, Liverpool reporting 4. For the same week Glasgow reported 10 deaths from diphtheria. There were 7 deaths from diarrhœa at Birmingham. Southampton, Barrow-in-Furness, and Wigan each reported 1 death from enteric fever. There were 14 deaths from measles at Belfast.

London, Glasgow, and Edinburgh each reported 5 deaths from cerebrospinal fever.

Deaths from influenza fell once more to 429 (512 last week). Of the 401 outside London 71 were reported from the south-eastern area; 202 from the northern area (Sheffield 35, Manchester 13, Liverpool 12, Bradford and Blackburn each 10); 92 from the midland area (Birmingham 16, Stoke-on-Trent 14, Nottingham 13, Bristol 10); 18 from the eastern area, and 14 from the south-western area. In the same week Belfast reported 13 deaths.

PARLIAMENT

ON THE FLOOR OF THE HOUSE

By MEDICUS, M.P.

THE last week of Parliament before the Easter recess touched its highest point on Tuesday when the Prime Minister reviewed the progress of the war. Mr. Chamberlain's speech and the debate as a whole were centred on the tragedy of the Finnish situation and many members were bewildered as to why Finland needed to capitulate if Great Britain and France were sending her such substantial aid as the Prime Minister detailed. The hard fact was that the Finnish command had got the time-table of the war wrong. Feelings in the debate got very heated and interchange of opinion and interruptions were frequent. Commander King-Hall amused himself and the House by his description of the Treasury Bench as consisting of the Prime Minister battleship, a battle-cruiser near him "not exactly stream-lined," and for the rest a set of "drifters, trawlers, dredgers and other auxiliary vessels." On which Commander Southby interjected "And with a submarine below the gang-way," which is where Commander King-Hall has taken up his seat. When the Prime Minister wound up the debate which he had begun—a formidable undertaking for any man—he was able to announce that the raid on Sylt was in progress. The news of this was sent by wireless from the scene of action and while the House was discussing it the fighting was on. An incident like this roused the House to a vivid interest and the news was received with a cheer. Then Mr. Chamberlain returned to the war on the House of Commons front and accused the leader of the Liberal Opposition, Sir Archibald Sinclair, of being "peevish when he was interrupted" as well as perverse and ungenerous about the offer of help to Finland. He ended his speech by saying that he accepted and subscribed to "the words used the other day by President Roosevelt as to what a peace should be."

The last day before the recess was taken up by a debate on the report of the West Indies Commission, the main recommendations of which the Government has undertaken to implement. These are far-reaching and involve the expenditure of a great deal of money on various forms of welfare work and the setting aside of money for research. Whether the chronic demoralisation of the West Indies economic position will be cured by these means seems open to doubt. One interesting feature of the West Indies problem is that despite great poverty the population is increasing very rapidly. The ameliorative service set up by the welfare scheme will improve conditions and presumably stimulate the growth of population still further, when the pressure of the economic situation will become more severe. The West Indies seem likely to provide an interessting chapter in eugenic experience.

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The House has got into the habit of taking first-class ministerial statements in answer to questions without blinking. This week Mr. Geoffrey Lloyd, Minister of Mines, announced in answer to a question the setting up of inquiries into "six specific problems" concerned with the substitution of important fuels by home-produced fuel, the work to be carried out by six separate committees. These proposals arise out of the report of a scientific and technical advisory committee under the chairmanship of Sir William Bragg, P.R.S. and the committees now appointed coruscate with scientific and technical talent. If peace would only act as quickly as war!

Another important statement was by Sir John Anderson announcing a temporary arrangement for meeting cases of hardship "arising as a result of the existing scales of Workmen's Compensation pending the inquiries of the Royal Commission." As a simple plan, not necessitating a "means test" (its avoidance is a significant comment on the old-age pensions debates) the Government propose to give supplementary allowances. These will be of 5*s.* in respect of the man's wife and 3*s.* in respect of each of his children under fifteen years of age with an over-riding maximum of seven-eighths of the man's loss in weekly earnings. These and similar problems are now being dealt with very expeditiously. Parliament certainly works more quickly in war than in peace.

The Medical Parliamentary Committee, continuing their work of keeping up to date in all matters into which medical questions enter, visited Orpington Emergency Hospital and the hospital in the Royal School of the Blind at Leatherhead on Tuesday. Criticisms were few, the main one being of the difficulties caused by dual control between the county authority and the institution concerned.

Parliament is to meet again on April 2 and the Budget is to be opened on April 23.

FROM THE PRESS GALLERY

Some Comments on the Health of the Troops

IN the course of a debate on March 14 Rear-Admiral BEAMISH said that some men having passed through a medical examination found themselves, with the best will in the world, incapable of supporting the strain of military training. He believed that if these were weeded out the Army would be more efficient. The report of the conference called by the Ministry of Pensions, over which Lord Horder presided, requested that during the period of training men should be carefully watched and that those who showed any indication of nervousness or mental instability should be reported upon and weeded out of the Army. They could only be a danger to themselves and to the other people with whom they were serving. He felt sure that a certain number of such men were slipping past the medical boards.—Mr. GLENVIL HALL also expressed some apprehension that, in spite of the fact that the R.A.M.C. wanted to do its job properly, a number of men were finding their way into the Forces who were quite unfit. He referred to a statement of the Secretary of State for War that if osteopaths also possessed a medical degree he would be willing to consider the use of their services when possible. Mr. Hall claimed that it was an old-fashioned view to imagine that members of that profession could be of little use to the Services unless they also had a medical degree.

Miss WARD urged the Secretary of State to examine the question of the nursing of troops being put into the hands of the Ministry of Health. She did not think that a division of responsibility for nursing made for efficiency, and it would be much more satisfactory if the whole of the hospital arrangements were in the hands of the War Office. It would be more suitable and more efficient if there was some hospital accommodation, between the big civil hospital type and the small regimental type, on the lines of the hospitals which were established in the last war.

Sir FRANCIS FREMANTLE did not think it was always recognised that the prime duty for the health of the troops was not merely the treatment of the sick but keeping them healthy and making them stronger both morally and physically. He was glad that the Secretary of State had pointed out that the responsibility for the health of the troops did not lie primarily with the medical officer but with the commanding officer. He sympathised with the War Office and their officials in regard to the publication of complaints which were unsubstantiated by facts. It had been shown that 80 per cent. of the complaints brought to a certain responsible quarter had been proved to be without foundation. A member of the House had been informed, on what seemed to be most reliable information, that in a military hospital there were 140 deaths from pneumonia, but investigation showed that there were only 3. The spreading of such statements devoid of reality was disgraceful. There must be some mistakes, but so far as the Parliamentary Medical Committee had examined them there were few that could be attributed to real neglect, and very few causing great suffering. Rehabilitation in theory and practice was, he said, most important, especially in the case of fractures. The same thing was required in the military service. Men should not be kept hanging about doing nothing, and they must distinguish definitely between the period when the men felt really ill and the period of convalescence. In this war, contrary to previous practice, when soldiers were invalided home from overseas they went into civil hospitals under the Emergency Medical Service. That had great advantages, but also certain disadvantages. When a man was convalescing it was all to the good, if he was going back to Army life, that he should be under military discipline and be rehabilitated. He hoped that a clear distinction would be kept, because when the soldier was really incapacitated it was no question of discipline. Treatment in a civil hospital was as good as in a military hospital, and generally it was better. When a man got to the convalescent stage he should be removed to a military convalescent camp where he could be rehabilitated. The rehabilitation scheme ought to be extended under the Ministry of Pensions to those who could not return to duty and should be worked in combination with the civil schemes. Papworth was a concrete example of the kind of rehabilitation which they all desired to see.

Mr. OLIVER STANLEY, Secretary of State for War, replying to the debate, referred to the point raised by Miss Ward about the relationship between the military and the civilian sides in existing hospital arrangements. He said that he did not regard it as altogether satisfactory. It was a plan which was laid down when the whole emphasis was on bombing, and civilian casualties which would result from bombing, rather than on land warfare and the military casualties resulting therefrom. He was in the middle of a discussion with the Minister of Health to see whether it was possible to make modifications which would still leave hospitals able to accommodate civilian casualties, but at the same time give more control and greater certainty, not only as regards the number but the allocation of beds which were required for military casualties.

Workmen's Compensation

In answer to a question on March 18 Sir JOHN ANDERSON said that the Government had devised a temporary scheme for meeting cases of hardship arising as a result of the existing scales of Workmen's Compensation pending the inquiries of the Royal Commission. It was apparent that any temporary measure, to be brought into operation speedily under war conditions, must be simple, not involving any large changes in the structure of the existing system and unlikely therefore to prejudice any proposals which the Royal Commission might make. The Government also regarded it as important not to introduce into the existing scheme a procedure which involved inquiry as to means, such as would be unavoidable if an attempt were made to adjust benefits to the degree of hardship in individual cases. The Government had decided to provide improved benefits for men with wives and young children, this being the class of people among whom hardship was most common. They proposed a supplement of 5*s.* for the man's wife and 3*s.* for each of his children under fifteen years of age, with proportionately reduced scales in cases of partial incapacity, and subject to an over-riding maximum of seven-eighths of the man's loss in weekly earnings. The supplement would be payable by the employer.

The supplement would not be limited to cases of accident occurring after the proposed legislation came into force. Sir John Anderson had received definite assurances that it would be the policy of the British Employers' Confederation to discourage discrimination against the employment of men with families on account of this supplement, and that the Accident Offices Association would make no such discrimination in the matter of insurance.

In the House of Lords on March 14 the Royal Assent was given to the Mental Deficiency (Scotland) Act.

The Old Age and Widows Pensions Act also received the Royal Assent.

QUESTION TIME

The Public Health

Mr. RHYS DAVIES asked the Minister of Health whether his medical advisers had noted the recent unparalleled increase in sickness in this country; and whether he was taking any steps to prevent a recurrence.—Miss HORSBRUGH replied: The phrase used in the question would give, I think, quite a mistaken impression. Influenza has been prevalent in recent months, though the largest number of deaths in any one week has been 629 (for the week ending February 24) which compares favourably with the maximum for 1933 (1934 deaths) or for 1937 (1155 deaths). There has also been a considerable prevalence of cerebrospinal fever, but owing to new methods of treatment the mortality-rate has been considerably lower than in the past. The experience of this winter has been, for most diseases, actually more favourable this year than in the year previous.

Effect of the Blackout on Public Health

Sir HENRY MORRIS-JONES asked the Minister whether any investigations were being made by his department into the deleterious effect on the health of the people owing to lack of proper ventilation because of the blackout; and, if so, what was the result of this investigation.—Mr. WALTER ELLIOT replied: Attention is being paid to the effect on the health of the people, of abnormal conditions created by the war, of which the blackout is one, but no special investigations of the nature suggested have been undertaken.

Sir H. MORRIS-JONES further asked the Home Secretary whether his department had conducted any experiments to secure better ventilation in houses, factories, offices and public buildings during the blackout and, if so, with what results.—Sir JOHN ANDERSON replied: Experiments have been carried out by my department, and it is proposed to issue shortly a pamphlet on factory ventilation in the blackout, and specifications of means of ventilation suitable for houses, offices and public buildings.

Sir FRANCIS FREMANTLE: Does this apply to air-raid warden posts, which are very badly ventilated?—Sir J. ANDERSON: Those have been attended to for the most part.

X-Ray Examination for T.B. in the Services

Miss WARD asked the Secretary of State for Air whether, in view of the Admiralty's decision to examine naval personnel by X ray to ascertain whether there were any tuberculous tendencies, he would adopt a similar policy for the Air Force personnel.—Sir KINGSLEY WOOD replied: This question is now under consideration.

In reply to a similar question addressed to the Secretary of State for War, Sir V. WARRENDER replied: Consideration is being given to this matter, but in the case of the Army serious difficulties are involved.

Committee of Consultant Advisers

Sir ERNEST GRAHAM-LITTLE asked the Minister of Health why a distinction was made between the English and the Scottish representatives on the committee of consultant advisers to the Emergency Hospital Service, seeing that the latter gave their services without payment and the former did not.—Mr. ELLIOT replied: I think there must be some misapprehension. There is no committee of consultant advisers. The information which I gave in reply to a question on Feb. 8 expressly related only to England and Wales. I am satisfied that the time which the consultant advisers in England and Wales are required to give to their duties is such as fully to justify the payments made to them. The arrangements made in Scotland are a matter for the Secretary of State for Scotland.

Mobile Surgical Teams

Mr. GROVES asked the Minister whether emergency mobile surgical teams, to operate wherever needed, had been organised in England as well as in Scotland.—Mr. ELLIOT replied: Yes. These teams, which are essential in order to secure the necessary economy in medical personnel, have been organised in both countries.

Psychological Treatment after Air-raids

Mr. GROVES asked the Minister whether the services to be provided by medical practitioners for air-raid casualties at 16*s.* a year would include psychological treatment.—Mr. ELLIOT replied: Subject to the conditions set out in the published memorandum the scheme covers any domiciliary medical attention which is required as the result of the air-raid injury.

British Social Hygiene Council

Mr. JOHN MORGAN asked the Minister if he was aware that the British Social Hygiene Council was in danger of ceasing to exist for want of Government and public financial support; and was he prepared to provide advisory and publicity services dealing with the particular aspects of public health hitherto covered by this organisation or to assist the organisation to carry on its work.—Mr. ELLIOT replied: I am aware that financial difficulties have been experienced by the council, and I have drawn the special attention of local authorities responsible for education in social hygiene to the value of the facilities provided by the council in discharging their responsibilities.

Soldier's Death after Vaccination

Mr. ALFRED EDWARDS asked the Secretary of State for War if he had now considered the case of Dennis Barnes, who died following vaccination; and if he could now make a statement.—Mr. OLIVER STANLEY replied: Gunner Barnes was vaccinated by the medical officer on Dec. 28th. No form of threat or pressure was used. The soldier at no time reported sick, and he was on parade on the morning of Jan. 27. He was billeted at his own home, and on the morning of Jan. 28 he was reported by his father to be very ill. A Royal Army Medical Corps officer went with the father immediately to the house and found that the soldier was dead. The matter was reported to the coroner, who arranged for a post-mortem examination by the pathologist of the East Suffolk and Ipswich Hospital. The pathologist was asked to consider carefully whether the fatal infection was in any way connected with the vaccination, and stated that the cause of death was a streptococcal infection which he did not think obtained entrance through the vaccination mark. The vaccination scab appeared quite healthy. In view of this report, the coroner did not consider it necessary to hold an inquest.

BISMUTH BY MOUTH FOR SYPHILIS

WITH reference to our leading article of March 16 Messrs. Eli Lilly write: Some confusion may arise from the statements "Meininger and Barnett found that the optimum daily dosage was six capsules each containing 0·2 g. of the drug," and "Scholtz, McEachern and Wood regard four capsules, or 0·8 g. of sobisminol as an adequate daily dosage" when these doses are considered in relation to the product now commercially available. Actually the capsules used by the American workers (*J. Amer. med. Ass.* 1939, **113**, 2214 and 2219) contained "the reaction product of sodium bismuthate 0·2 g., trüsopropanolamine 0·4 g., propylene glycol 0·1 g. and ethyl alcohol 0·1 g." representing approximately 150 mg. of elemental bismuth, and Scholtz, McEachern and Wood reported that "six capsules, or about 0·84 g. of bismuth daily . . . was used as the standard dose." In quoting this dosage you have inadvertently given the number of capsules as four. The description of the capsules used in the early work appears to be identical with that of the product now available. Both groups of workers seem to have reached the conclusion that six capsules, each containing approximately 0·75 g. sobisminol, or a total of 4·5 g. of the drug, represented the optimum daily dosage. In view of the importance of adequate dosage it should be made clear that the daily administration of 0·8 g. of sobisminol, which might be inferred from your article as being a suitable dosage, would in point of fact be virtually useless.

LETTERS TO THE EDITOR

THE BIRTH OF THE E.M.S.

SIR,—Sir Ernest Graham-Little has got his facts wrong. The committee appointed by Sir Samuel Hoare in the spring of 1938, of which I have the honour to be chairman, presented an interim report dated July 20, 1938; it did not meet again. This committee did not touch on personnel until its final meeting, when it had to be content with a rough estimate of the calls likely to be made on the profession in London; it ventured to draw only one conclusion from these figures, namely that mobile surgical teams would be required. The committee had therefore nothing to do with the relative merits of whole-time and part-time service; it did not even discuss them.

This committee, too, was not responsible for the policy of degrading the London hospitals. The casualties were to be treated in London (perhaps our prescience owed something to the lack of a decent alternative at that time). The London hospitals were to be casualty clearing stations, not mere ambulance posts as at present; their existing accommodation was to be substantially increased by additional beds; one teaching hospital, I remember, more than doubled its beds in the plan. Medical education was not discussed; in our scheme things went on as before. There was no question of the dispersal of students; they were needed in London.

So much for the facts; a word on panic. It was said by an unfriendly critic of those for whom we worked in Whitehall in the summer of 1938 that they could not believe in the possibility of war, since they went about as if they had all eternity to complete their plans. However unfair that may be, it would be ridiculous to charge them at that time with panic. After July 1938 I was only a pawn in the game and I can speak with detachment of policies I could no longer effectively influence. The evacuation of the London hospitals, of school-children and of the Civil Service were part of a deliberate policy of the Government based on the advice of the Air Ministry. Doctors who were called in by the Ministry of Health or by the Home Office were not asked if they agreed with that policy: the Government and the Government alone was responsible for the measures castigated by Trotter.

Trotter's contribution on "Panic and its Consequences" fell into two parts: a simple dissertation on panic which was unexceptionable; and the application of this to the measures taken by the Government which was much less secure. He wrote, "It was generally believed that a first-class air-raid might kill 50,000 and wound 300,000 more." Did *anyone* believe this? He would have been the first to agree that panic and exaggeration are half-brothers. I can imagine how Trotter himself would have dealt with that dialectical device "it was generally believed" if used by another. Again, the German military command was "little likely to waste its strength on excentric blows that could not be followed up." I venture to doubt whether we have sufficient facts at the present time to speculate with profit on the reasons why Germany has not bombed London.

I remember once, when I was ill, Trotter walked into my bedroom. He had come in his kindly way to discuss a paper I had written on the medical curriculum; he made a flattering proposal that we should join forces to get something done. But I listened for an hour to a logical plea for a return to the apprentice system; he meant merely that there was a danger we might become too laboratory-minded. When I read his charge that the Air Ministry had acted from panic—he must have known who was responsible for the measures to which he took exception—there came into my mind an occasion at Andover when, in the middle of a lecture to the R.A.F. Staff College on the moral factor in war, I was suddenly seized with the incongruity of a middle-aged apothecary haranguing those young toughs on such a theme.

I am, Sir, yours faithfully,

C. M. WILSON.

PEPTIC ULCER IN THE SERVICES

SIR,—It seems quite clear from Dr. Izod Bennett's letter that, though, as he says, his experience of peptic ulcer has been wide, it has not included a series of patients who have had a partial gastrectomy or gastroduodenectomy performed for this condition. If it had he would know that, after the operation, patients become apparently normal individuals. They live ordinary lives and eat ordinary food; they are not aware that they have stomachs. I have known a labourer perform the hardest physical work, digging the soil and wheeling it in a barrow up an incline, four years after a partial gastrectomy for a penetrating ulcer.

The policy of discharging from the Army all soldiers with peptic ulcers is not only short-sighted, it is not humane. Nobody can say whether, after these operations, soldiers would be able to withstand the rigours of a winter campaign, but civilian experience suggests that many of them ultimately would be. All I can affirm is that in civil life many patients suffer no handicap whatever.

Dr. Bennett will agree, I know, that the problem seldom arises in young recruits. Chronic peptic ulcer is rather a disease of middle life. The study of the results of resection operations for peptic ulcer would, I am sure, be a revelation to him. That Dr. Bennett, with his vast experience, is quite unfamiliar with these cases can only be explained on the assumption that they are so well that they never have occasion to consult a physician.

I am, Sir, yours faithfully,

Basingstoke. CHARLES A. PANNETT.

BISMUTH BY MOUTH FOR SYPHILIS

SIR,—The leading article in your issue March 16 on the successful treatment of syphilis by the mouth should prove of particular interest to our Crown Colonies and overseas dependencies, where the venereal and associated diseases are a much more serious problem than they are at home. I know that statistical returns are a dull means of illustrating facts but I think few people really realise how severe this incidence may be. Thus in Nigeria, for instance, the annual medical report for 1934 shows that, out of a total of a little over 555,000 non-European attendances for the year, for all disease, approximately 13,000 were for syphilis and no less than 130,000 for yaws, nearly a quarter of the whole official return. The same report states that about 16,000 cases of gonorrhœa attended also. This latter figure represents the merest fraction of the true incidence, the attitude of most patients being one of indifference at that time owing to the absence of any specific cure (before the introduction of sulphanilamide &c.).

It is interesting to compare these returns with those for leprosy for the same period. In all, inclusive of

missions, the total figure receiving "colony treatment," which is in actual fact the only sound individual type of treatment they can get, was 6000, less than 3 per cent. of the estimated figure—namely, 200,000 for the colony. The effect of endemic venereal or other contagious associated non-venereal disease on the current living standards is very great, owing to loss of labour time and so on. This aspect is also worthy of consideration in relation to improvements recently suggested by the Colonial Office.

If therefore Sobisminol is to be established as a specific for the treatment of both yaws and syphilis by the mouth, it could prove of great value. Not least important perhaps is the fact that injection therapy may never become very popular in some Mahommedan areas on deeply-felt religious grounds, on account of the possibility of scarring or in the case of intramuscular injections even of mutilation. This partly explains the fact that in Nigeria syphilis, which is very common among the Mahommedan Hausa, is not nearly as fully treated as is yaws, which though geographically defined is so common in the south. Syphilis is comparatively uncommon in the south. Gonorrhœa is widespread throughout the whole of Nigeria, an index, like tuberculosis, of faulty living standards.

I am, Sir, yours faithfully,

Parkstone, Dorset. D. FITZGERALD MOORE.

INFECTIVE HEPATITIS AND CATARRHAL JAUNDICE

SIR,—In opening the annotation on this subject in your issue of March 23 (p. 558) you say: "It is now accepted that there are two forms of mild jaundice in this country, one due to a catarrh of the common bile-duct associated with duodenitis, the other to hepatitis." So dogmatic a statement may well stir up controversy. The division you quote is due largely to Hurst and Simpson [1] and is by no means generally accepted. Cullinan [2] and Pickles [3] reject the division as applied to epidemic benign jaundice. The clinical pictures described as characteristic of the two types may both appear in a single epidemic, and Quick [4] finds biochemical evidence of mild hepatic necrosis in cases clinically diagnosed catarrhal jaundice.

As long ago as 1912 Cockayne [5] cast doubt on the theory of an upward spread from a primary duodenitis, and a comparison of those icterogenic diseases whose pathology is better understood brings into evidence the rarity of the ascending route to the liver. Ascaris may occasionally occupy the common bile-duct, but ascending cholangitis seems very rare except as a complication of gross calculous cholecystitis or advanced malignant disease. Even when, as in enteric and some cases of spirochætosis icterohæmorrhagica, the virus is first ingested, jaundice is caused after invasion of the blood-stream. The conception of jaundice resulting from simple biliary catarrh is steadily losing favour.

Not everyone will agree with your statement that infective hepatitis is spread from one person to another by droplet infection. The evidence is as yet inconclusive. The impression that the disease is commonest in partially closed communities may well result from the greater readiness with which such outbreaks are studied.

Others will probably question the criteria which you advance for distinguishing benign from leptospiral jaundice.

You conclude with a subject of great interest—Findlay's recommendation of the administration of glucose to *all* cases of infective hepatitis as a prophylactic against acute necrosis of the liver. Research in America into the causes of arsphenamine jaundice revealed that a high carbohydrate diet was, surprisingly, a predisposing cause of this type of liver necrosis, and that the liver could be fortified by a diet rich in fats. Since you indicate that arsphenamine jaundice may come to be classed as an infective necrosis of the liver, you may consider the matter of sufficient importance to merit an amplified account of the present position in this dietetic conflict.

I am, Sir, yours faithfully,

The Lizard, Cornwall. R. E. HOPE SIMPSON.

MINERS' NYSTAGMUS

SIR,—With reference to the recent discussion of the ætiology of miners' nystagmus, the following observations of miners on the Bengal and Bihar coalfields may be relevant. In connexion with health investigations carried out for the Government of India I had the opportunity of examining a large number of Indian miners, but never saw any sign of nystagmus nor could obtain any record of the condition having been noted by others. The men were generally drawn from primitive agricultural communities, and came to the coalfields for a period of several months at a time. They were often unwilling to work more than four days a week. A less cramped posture was maintained while at work than in this country, since the seams of coal were of greater depth. The lighting was very poor. The people with whom I talked had never heard of compensation for nystagmus amongst miners.

I am, Sir, yours faithfully,

Oxford. DAGMAR CURJEL WILSON.

VITAMINS IN MARGARINE

SIR,—Medical men incur a certain amount of responsibility towards their patients in recommending to them special articles of diet. It was announced that from Feb. 5 all margarines would contain an added amount of vitamins A and D equal to that in butter. Certain brands have for some time had these vitamins added, to an amount, according to the manufacturers' statements, equal to that in summer butter. Now that many other manufacturers of margarine, not necessarily possessing laboratories, are included in the general statement issued by the Ministry of Food, one would like to know whether the process of manufacture destroys the activity of added vitamins, and by what tests of the finished article and methods of inspection the standard is maintained.

I am, Sir, yours faithfully,

Great Kimble. ROGER N. GOODMAN.

*** We understand that it is not a difficult matter to dissolve the vitamin concentrates in part of one of the oils used for the fatty mixture which is the basis of margarine. In this way thorough mixing is obtained and the subsequent emulsification makes it certain that the whole blend is uniform. The known stability of the added vitamins A and D justifies the assumption that under ordinary conditions there is no appreciable deterioration during the period between manufacture and retail sale.—ED. L.

1. Hurst, A. F. and Simpson, C. K. *Guy's Hosp. Rep.*, 1934, **84**, 173.
2. Cullinan, E. R. *Proc. R. Soc. Med.* 1939, **32**, 933.
3. Pickles, W. N. *Lancet* 1939, **1**, 893.
4. Quick, A. J. *Brit. med. J.* 1938, **2**, 683.
5. Cockayne, E. A. *Quart. J. Med.* 1912, **6**, 1.

OBITUARY

PATRICK LAIDLAW

K.T., M.B. CAMB., F.R.C.P., F.R.S.

THERE will be many who grieve to learn of the death of Sir Patrick Laidlaw on March 19 at the age of 58. He had been working in his laboratory to within a few hours of his sudden but peaceful death. His place will be hard indeed to fill either as a colleague or on a committee or in any capacity where experience and wise judgment are needed, for his knowledge covered an unusually wide field in medicine and the kindred sciences.

Elliott & Fry

Patrick Playfair Laidlaw, the son of Dr. R. Laidlaw, who was medical officer in the Seychelles, was born on Sept. 26, 1881. He was educated at the Leys School and St. John's College, Cambridge, and thence went to Guy's Hospital. He never had robust health, one leg having suffered from an attack of poliomyelitis in his youth. While still a student at Cambridge he published four papers on anatomy and one on blood-pigments. After a few years as demonstrator of physiology at Guy's he joined the staff of the Wellcome Physiological Research Laboratories in 1909. There then began the first of the two most fruitful periods of his life, the pharmacological chapter. In this he was associated chiefly with H. H. Dale—an association which was to continue for almost all his life—and with A. J. Ewins. During the next five years he published, alone or with his collaborators, twenty-five papers on pharmacological subjects. Amines were the chief object of study, and his work with Dale on histamine is classical. In 1914 he returned to Guy's to become Sir William Dunn lecturer in pathology, and he remained there throughout the war and until 1922. He was not really happy in teaching and his greatest contributions during that period were his initiative in devising methods for the anaerobic culture of bacteria and his work with Dale and Richards revealing the rôle of histamine in shock.

The second important chapter in Laidlaw's life began in 1922 when he joined the staff of the National Institute for Medical Research soon after its establishment at Hampstead and Mill Hill. A programme of research on virus diseases had just been put in hand. Support for investigation into dog-distemper was forthcoming from a fund raised by the *Field*, and the study was undertaken by Laidlaw in collaboration with G. W. Dunkin. The difficulties were considerable; because of the infectious nature of the disease, it was found necessary to raise a stock of distemper-free dogs. Progress was helped by the discovery, which followed a clue provided by the late Captain S. R. Douglas, that ferrets were uniformly susceptible to dog-distemper. Thereafter the secrets of the disease were unmasked in an orderly manner: first, in 1926, the features of the uncomplicated disease in the dog and in the ferret were described; then came the confirmation of Carré's claim that the responsible agent was filtrable, next the successful immunisation of ferrets and of dogs with formolised vaccines, and finally, in 1931, the discovery of the value of immune serum. There can be few examples of a disease in which one team of two workers has added so much to our knowledge of its causation and followed up such discoveries by finding how to apply them fruitfully in practice.

It was in 1933 when the distemper discoveries were being thus applied more widely and the need for fundamental research on that disease had lessened that Laidlaw, working now with Wilson Smith and C. H. Andrewes, found that ferrets were susceptible to infection with a virus from cases of human influenza. In the following years his wide knowledge of many branches of medical science, together with the experience gained in the work on distemper, proved invaluable in making headway in what proved a more difficult study than dog-distemper. In 1936, on the death of S. R. Douglas, Laidlaw became deputy director and head of the department of experimental pathology of the National Institute. Thereafter he took a less active part in the influenza work but continued to be a fountain of freely given help and inspiration to the rest of the team, as well as to many others.

While engaged on his studies on virus diseases he found time for work leading to valuable contributions on the chemistry of the tubercle bacillus (with H. W. Dudley) and on the action of emetine on amœbæ (with C. Dobell). Besides all this, there was much work which never led to publication. Again and again he tried some new and ingenious plan to grow viruses in non-living culture media; when it failed he would be back to the attack with another scheme within a few months. He found characteristic inclusion-bodies in dog-distemper, but refused to publish his findings when he unearthed a paper by Sanfelice who had described the same appearances nearly twenty years earlier—even though that work had meanwhile been almost entirely overlooked. Nor did he ever publish the staining method he devised to reveal those inclusion-bodies. His last publication, the Rede lecture delivered in 1938, reviewed our knowledge of virus diseases and contained important suggestions as to the nature of viruses. Viruses, he argued, might be degraded micro-organisms, stripped of all or almost all their enzyme-systems, "living a borrowed life" in the cells they parasitise. Since last September he had been working enthusiastically on fresh problems in the field of infectious disease and had communicated his enthusiasm to the colleagues working with him.

Laidlaw's outstanding contributions were recognised by his election to the Royal Society in 1927, the award of its Royal Medal in 1933, his election as F.R.C.P. in 1934 and his knighthood in 1935. Only a day or two before his death he had heard with pleasure that he had been elected an honorary fellow of his old college at Cambridge—St. John's.

Sir Henry Dale writes: In the judgment of those who have been in touch with the progress of medical research during the present century, Laidlaw's pioneer work on virus infections will probably rank as his most important contribution to the advancement of knowledge. I think that it should do so. When he came to the National Institute, in 1922, work in that field was a new adventure, not only to him but to most pathologists, and a large part of the methods now in daily use had yet to be discovered and elaborated. The advance has been so rapid since that date, and

has been aided so much by friendly interchange and collaboration, even between those working in different countries, that it is less easy here than in some other fields of research to attribute particular items of method to individual discoverers. Laidlaw would certainly have been the last to put in a claim for any detail, or to allow it to be made for him. I think it is sufficient to recognise that, with good co-workers to whom he would have given much of the credit, he tackled in succession two of the major infective diseases of animals and men, dog-distemper and influenza, overcame difficulties which had baffled many predecessors and would have discouraged most men from further attempts, and with such success as not merely to establish the viral origin in both cases, but to lay down the lines of prophylaxis. A sufficient achievement surely, by itself, to keep his name in grateful honour. But I think that it was an important factor, even of his success in this field, that Laidlaw was so much more than a specialist on virus studies, or than a general pathologist in any conventional sense. His first published research, undertaken on his own initiative while still in his student's science course at Cambridge, was a little classic in biochemistry. At a later, intermediate stage in his career, I had enjoyed, over a period of happy years, his perfect and inspiring collaboration in researches ranging over the borderlands of pharmacology, biochemistry and experimental pathology. Very few men, indeed, have had Laidlaw's range of knowledge, equipment and eager interest in the medical sciences, or his fertility in ideas and devices. There must be very many cases in which the clue, which has enabled others to reach an important objective, has been given by Laidlaw in verbal suggestion, or in some modest, half forgotten note. Even the occasional glimpses, which shyness and dislike of self-assertion made it difficult for him to afford, must have given to those who met him less frequently some hint of the riches of his mind, and of the quiet generosity and steadfastness of his character. We who for many years have had the great privilege of daily work with him, have come to depend so much on his knowledge, on his sane and kindly criticism, on his ungrudging help and his unwavering friendship, that we find it difficult, indeed, to face the future without him.

GEORGE WILLIAM AUGUSTUS LYNCH

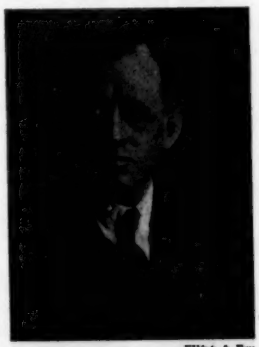
M.B. CAMB.

Dr. Lynch, a distinguished medical administrator in Fiji, died on March 22. He was the son of William Nicholas Lynch, barrister of Georgetown, British Guiana, and was born in London in 1861. From Westminster School he went to Caius College, Cambridge, and St. Thomas's Hospital, where he qualified in 1885. Five years later he was appointed district medical officer of Ba, Fiji, and in 1897 he became senior medical officer in the Colonial Service in that colony and was resident medical superintendent of the Colonial Hospital at Suva. In the next few years he published a few papers in THE LANCET and elsewhere on filariasis and epidemics among the Fijians and in 1908 was made chief medical officer, a member of the legislative council and chairman of the Central Board of Health. He became, in fact, writes a colleague, an institution in Fiji and his memory will be cherished with affection by those who served with or under him during his long and successful regime in the colony. He retired after 30 years in the Colonial Service and for a few years after his return home practised at Aldeburgh, Suffolk. He leaves a widow and one daughter.

EDWARD MAPOTHER

M.D. LOND., F.R.C.P., F.R.C.S.

THE death of Dr. Mapother removes a leader of English psychiatry. His position at the Maudsley Hospital enabled him, in the interval between two wars, to influence the whole trend of psychiatric development as this formerly neglected branch of medicine came to take its proper place. Between the extremists—those who believe that everything that is not physical must be fairy-tale, and those who think psychopathology is the alpha and psychotherapy the omega of psychological medicine—he steered a well-planned and progressive course.



Elliot & Fry

Edward Mapother came of an English family that had been settled in Ireland for three centuries. He was born in Merrion Square; his father, Edward Dillon Mapother, was a distinguished anatomist and president of the Royal College of Surgeons in Ireland. The family moved to England when Mapother was young and his education was entirely in this country. But his Irish origins betrayed themselves in his wit and pugnacity which often found expression in the trenchant phrases of obviously enjoyed controversy. Mapother's attachment to University College and University College Hospital, his alma mater, was strong, and nothing gave him keener pleasure than his election to a fellowship at University College three years ago. He was an able student, carrying off medals in anatomy and physiology, and later in medicine and pathology. He qualified in 1905 and acquired, as house-physician to Risien Russell, that appreciation of clinical neurology which influenced all his psychiatric outlook and was to be expressed, towards the end of his life, in his hope that a neurological wing might be built at the Maudsley to make it a true centre of neuropsychiatry. The hope had not been realised when war broke out, but Mapother believed that without such a synthesis both psychiatry and neurology must suffer. His conception of the theory of psychiatry was based on the conviction that rules found to be applicable to neural function must also apply in medical psychology; he developed the theme in his Bradshaw Lecture to the Royal College of Physicians in 1936, and he had intended to embody it in a larger work as soon as he had leisure after his resignation from the onerous position at the Maudsley. Such thoughts and plans were, however, far from his mind when in 1906 he began to work for his M.D., which he obtained in 1908, and for his F.R.C.S. which was acquired two years later. He spent the intervening time as a locum tenens in various mental hospitals, where discerning colleagues persuaded him to make his career in psychological medicine. He joined the staff of Long Grove Asylum, then recently opened by the L.C.C. with Hubert Bond as medical superintendent and Bernard Hart, Henry Devine and other distinguished psychiatrists among its medical officers.

He remained there until 1914, when he joined the R.A.M.C. He served in Mesopotamia and in France, returning to England in 1917 to organise the neuro-

logical division of the 2nd Western General Hospital. He was in command there until 1919, and was then appointed medical superintendent of the Ministry of Pensions hospital for war neuroses established in the building designed to be the Maudsley. In due course the ministry gave up the hospital to its proper purpose and when it was opened, in 1923, as a centre for treatment, research and teaching, Mapother was selected to be the medical superintendent. From the beginning he took a long view of what he had to do. The three functions, which Henry Maudsley had stipulated, must go hand in hand: if they were to be fulfilled there was need of sound medical principles, an energetic, able staff, and the support and understanding of those who controlled the hospital financially and administratively. The extent to which he achieved his ends is the measure of his ability: it is well known that at the Maudsley the clinical work was sound and of a high integrity: the staff included many, if not most, of the ablest of the younger psychiatrists: and the L.C.C. proved generous and far-sighted in support of the hospital's work. The University of London recognised the achievement and the part Mapother played in it by appointing him three years ago to the newly-created chair of clinical psychiatry, tenable at the Maudsley. The Rockefeller Foundation endowed research at the hospital on a generous scale and provided opportunities for the members of the staff to acquire further experience abroad: the Commonwealth Fund of America also provided research fellowships there.

All this must be reckoned as Mapother's doing, for he gave all his abilities and effort to the hospital and thought only of its advancement, and thereby the advancement of psychiatry. He believed that a university clinic such as the Maudsley was must be not only a training ground for the doctors of the mental hospital service with which it was fortunately connected, but also a centre of active investigation in all the major departments of psychiatric research; a centre where trustworthy methods of treatment are fully employed, and experimental or limited methods used with responsible restraint; a centre with much more than a local sphere of influence. He carried this belief into his active encouragement of child psychiatry (he was an energetic member of the Child Guidance Council), of psychiatric social work (for which the Maudsley provided the training in adult psychiatry), and of occupational therapy. He was able to bring about a great increase in the facilities for outpatient psychiatry through the opening of clinics at municipal hospitals in London; he was also quick to see the possibilities of the observation wards for psychiatric education. He was concerned too in raising the level of undergraduate training, and instituted at King's College Hospital, where he was physician in psychological medicine, a series of lectures and demonstrations which covered several clinical years and provided an admirable foundation in practical psychiatry.

Mapother held many appointments. He was chief consultant to the Ex-Services Welfare Society and had, in consequence, an extremely wide acquaintance with war neuroses. This subject, head injuries and alcoholic mental disorders were the clinical topics to which he devoted special attention. He was consulting psychiatrist to St. Francis Hospital, to the Maida Vale Hospital for Nervous Diseases, and to the Queen Alexandra Military Hospital, Millbank. He was on the council of the Royal College of Physicians in 1937 and 1938. His services as examiner were constantly in demand by universities and by the Conjoint Board. He was on the council of the Eugenics Society, in whose work he took keen interest.

His health had been getting steadily worse for years and the last five or six winters he had had to spend abroad, as his asthma and the fibrosis of his lung made England impossible for him then. But he turned these enforced holidays to account: in Egypt he familiarised himself with the problems of drug addiction, and in India he visited the mental hospitals. In Ceylon he was invited by the Government to survey the existing arrangements; his masterly report, containing detailed suggestions for the reorganisation of the service, was printed by the Government as an official paper and might have been implemented but for the war. All these activities would have been impossible for him if it had not been for the constant help which he received from his wife.

Mapother was a man of strong opinions, strong contempts and strong loyalties. His feeling of responsibility towards his colleagues and towards medicine as a profession was remarkably intense: and for a man who had such polemical gifts and zest he was surprisingly ready to look at the opposite point of view, and free from rancour or malice. Towards the members of his staff he was always considerate and appreciative: he was proud of the men he had gathered about him during the fifteen years of his superintendentship, and he believed that through them he had assured the continuance at the hospital of those standards of progress and scientific probity for which he laboured.

AN APPRECIATION BY DR. F. GOLLA

At a moment when the tragedy of our civilisation has disintegrated and perhaps destroyed the institution that he loved so well, it might well be difficult to write about the influence of the work of Edward Mapother with the same note of glad confidence which would have sounded a year ago. For the now divided and evacuated Maudsley Hospital was not only Mapother's great work but it expressed the totality of his working life. Such doubts would however indicate a very short-sighted view. Whether the Maudsley as a unit stands or falls, the great service that Mapother rendered to British psychiatry was to actualise in this country the conception of the self-contained psychiatrical clinic as a centre for early treatment, teaching and research.

Only those who know the attitude of public authorities in this country towards the problems of mental disease and its treatment can appreciate the truly colossal task that Mapother undertook in obtaining support for his scheme and in reconciling hostile and reactionary influences. To this task he devoted almost his entire life. A brilliant clinician, he deliberately sacrificed most of the time that he would have liked to devote to the study of mental disorders to the unremitting and often distasteful work of a propagandist. Once he had decided that to obtain support for his projects was to do the most urgent and important work possible, he gave himself up to it with characteristic thoroughness. However much he might be pressed for time, however precarious his health, he maintained an untiring watch on all things that might affect his enterprise. No happenings even remotely connected with the Maudsley were allowed to escape his notice and every contact that held promise of eventual utility was cultivated. A true Irishman he had the national flair for politics and he succeeded beyond all expectations in attracting and reconciling the most divergent interests.

Naturally such work could only be accomplished at a price, and so far as he was concerned he felt that the sacrifice of his potential career as a physician was well justified. To obtain the support of reluctant authori-

ties and an inert university he found it necessary for the Maudsley to depart from the original plan of a centre for the intensive study of mental disease that had been the aim of Maudsley and Mott, and to enter on a more therapeutically dramatic and assertive career that in the view of many somewhat detracted from its utility as a home for research. Like most men who are single-minded in the pursuit of an unselfish end, Mapother had a certain streak of simplicity in his character that made him an indifferent judge of men. To all he applied the touchstone of devotion to his aim and he defended all those who professed allegiance to the Maudsley with an impetuous loyalty that was often a little disconcerting to colleagues whose detachment allowed a somewhat clearer view.

Mapother was a clinician of the first rank, a careful and acute observer; his work was characterised by a lucidity and objectivity that made attendance at his clinics a delight to all. Though like all the young psychiatrists of his generation he had at first been attracted by the Freudian theories he satisfied himself in later years of their utter inadequacy to deal with the problems of abnormal behaviour as he understood them and became a stout opponent of psycho-analytic methods. For philosophic thought he had little aptitude and his essays in that direction were unfortunate. Like the great psychiatrist Maudsley, Mapother was essentially an empiricist and this limitation really enhanced the objective value of his work. A life of such fierce energy left him little opportunity to conduct original work, and it is doubtful if he really grasped the purport of much of the more academic forms of research, but he had an unquestioning faith in the potentialities of science and it was due to his untiring efforts that the magnificent support of the Rockefeller Institute was given to the Maudsley. A fearless fighter he naturally aroused occasional antagonisms, but an opponent must have been blind indeed who failed to recognise that there was nothing of self-interest in the aims for which he fought.

It may well be that Mapother built far better than he knew. If the dream of a few psychiatrists should ever materialise and the London mental hospital service with its 35,000 patients and 14 mental hospitals should form one great psychiatric university drawing students from all over the world to its unequalled wealth of material, a university where all the centres collaborated for the common ideal, and where no one institution sought for predominance or eclectic seclusion, we should proudly and gratefully acknowledge that the work and courage of Edward Mapother had laid the foundations.

JAMES ABERNETHY

M.B. ABERD.

Dr. Abernethy died of meningococcal meningitis on March 10, less than a year after graduating at Aberdeen. He had been ill only twenty-four hours and his death at the City Hospital, where he was finishing his first house job, was a shock not only to his friends but to the whole profession in the city. After six years in Scotland he had planned a holiday at his home in Western Australia, hoping to come back to Europe with the Australian Expeditionary Force. While at college he was on the students' representative council and was a foundation member and eager worker for the Overseas Club—a club which in the last few years has made the idle hours of foreign students in that grey city much brighter. His cheerful frankness and charm had made him many friends in Aberdeen.

Miss Zoë Puxley has been appointed an acting assistant secretary of the Ministry of Health.

Medical News

University of Cambridge

On March 15 the following degrees were conferred:—

M.Chir.—A. H. M. Siddons.*

M.B., B.Chir.—K. P. S. Caldwell,* J. D. H. Iles,* N. B. Eastwood,* J. C. B. Nesfield,* L. M. Reid* and T. L. Stoate.

* By proxy.

The following examined for the final M.B. examination in 1940 have been appointed:—

Part I, *Surgery:* Mr. R. Davies-Colley, Mr. Julian Taylor, Mr. R. M. Handfield-Jones, Sir Alfred Webb-Johnson, Mr. Eric Crook. The following may be called upon to act: Prof. E. D. Telford, Mr. W. H. C. Romanis, Mr. W. D. Doherty, Mr. Reginald Vick, Mr. Lancelot Bromley, Mr. G. T. Mullally, Mr. V. C. Pennell, Mr. A. Tudor Edwards, Mr. R. H. O. B. Robinson and Mr. M. F. Nicholls.

Part I, *Midwifery:* Mr. L. Carnac Rivett, Dr. J. R. C. Canney, Mr. Aleck Bourne, Mr. A. Goodwin. The following may be called upon to act: Mr. L. H. W. Williams, Mr. A. J. McNair, Mr. H. G. Taylor, Mr. Victor Lack, Mr. Frank Cook, Dr. J. D. Barris, Mr. J. M. Wyatt and Mr. Clifford White.

Part II, *Medicine:* Dr. Geoffrey Evans, Prof. J. W. McNee, Dr. Crighton Bramwell, Dr. A. E. Naish, Sir Charles Wilson. The following may be called upon to act: Dr. C. E. Lakin, Dr. H. Gardiner-Hill, Dr. F. H. Young, Dr. A. C. D. Firth, Dr. J. M. H. Campbell, Dr. T. L. Hardy, Sir Adolphe Abrahams and Dr. Donald Hunter.

Part II, *Pharmacology, Therapeutics and Toxicology:* Dr. E. B. Verney, F.R.S., Dr. L. B. Cole, Dr. Philip Hamill, Dr. E. C. Warner, Dr. Clifford Hoyle and Prof. F. R. Winton.

Part II, *Pathology, Hygiene and Preventive Medicine:* Prof. H. R. Dean, F.R.S., Prof. Matthew Stewart. The following may be called upon to act: Dr. E. T. C. Spooner, Dr. E. R. Creed, Dr. Raymond Williamson and Prof. G. P. Wright.

University of London

Prof. F. R. Fraser has been appointed a representative of the faculty of medicine on the senate.

University of Sheffield

At recent examinations the following were successful:

M.D.—J. E. Edson and J. Pivawer.

FINAL EXAMINATION FOR M.B., CH.B.

Parts II and III.—John Wainwright (first-class honours); R. W. L. Hall, C. W. Lawson, and Arna E. Rides (second-class honours); V. H. Allan, Joy S. L. Allott, V. G. S. Damms, K. H. Hardy, J. E. Healey, J. D. Morgan, E. Robinson, R. A. Trevethick.

University of Leeds

At recent examinations the following were successful:

M.D.—I. D. Riley.

D.P.M.—M. Jeffrey.

FINAL EXAMINATION FOR M.B., CH.B.

Part II.—H. Petty and R. B. Zachary (first class honours); P. Austin, S. Long, E. E. Rawlings, R. E. Shaw, W. Thompson, and L. Watson (second-class honours); C. Bremer, G. Margaret Child, G. Collomosse, S. S. Freedman, Margaret D. W. Hamilton, E. G. Hardy, W. R. Heylings, G. H. Illingworth, D. H. Lambert, J. P. Lask, K. G. Marshall, Mary S. Nicholson, L. Rosenthal, R. A. Stamp, J. N. Stirling, I. M. Vites, W. K. J. Walls, H. D. Whiteley, H. A. Wilson, J. Wilson (*a*), J. Wilson (*b*), S. T. Winter, and S. Wray.

University of Liverpool

At recent examinations the following were successful:

D.P.H.

Part I.—D. Campbell, G. R. Thorpe, Lucy H. E. Walker, and G. Wynne-Griffith (new regulations).

D.M.R. & E.

Part A.—J. C. Kee, W. P. Stevens, S. W. Wherrett, and J. White.

D.T.M.

Alice Benjamin, P. Borg Mallia, M. P. Browne, Ruth F. Conway, L. H. Crosby, E. S. Dismorr, Frances Dooley, J. M. French, J. D. Fulton, D. B. George, W. R. Grant, Rebecca Koshi, Margaret P. Lyon, I. H. Marrable, J. D. Munroe, W. Z-A. Quraishi, L. K. Rittenhouse, H. V. ol M. Shaibany, I. Soorani, H. Stott, E. L. Tee, and A. H. Wright.

The A. H. Milne medal has been awarded to Dr. Alice Benjamin.

Society of Medical Officers of Health

The annual luncheon of this society will be held at the Piccadilly Hotel, London, W.1, on Friday, April 5, at 1 P.M. Mr. Walter Elliot will be a guest of honour.

Service Appointments

The following have been appointed temporary surgeon rear-admirals: C. P. G. Wakeley, E. L. Pearce Gould, R. A. Rowlands, J. W. McNee, G. Gordon-Taylor, Sir William Wheeler.

Port Regis Preparatory School

Sir Milsom Rees is offering five £60 scholarships at this school to sons of medical practitioners. Candidates must be under 9 years of age on June 11, 1940. Applications should be sent to the headmaster, Port Regis School, Broadstairs, Kent.

Extra Meat for Diabetics

Diabetics who wish to apply for an extra ration of meat should obtain a form from their local food office. This is in two parts, part A being for their personal and rationalistic particulars and part B a medical certificate. Their doctor must certify "that the patient named above is at present suffering from diabetes mellitus and is undergoing treatment under my care. The patient is being given . . . . . insulin per week." The dosage of insulin must be stated. There is no hint whether insulin is looked upon as a sine-qua-non, but presumably each case will be considered on its merits. Successful applicants may buy extra meat to the value of *1s.* 10*d.* a week per adult or 11*d.* a week for a child in exchange for their sugar ration.

Appointments

WRIGHT, H. J., M.B. N.U.I., resident assistant medical officer at Romsley Hill Sanatorium, Birmingham.

JOULES, HORACE, M.D. Lond., M.R.C.P., medical superintendent at the Central Middlesex County Hospital.

PETERS, L.B., M.B. Durh., temporary assistant school medical officer for Plymouth.

VARTAN, KEITH, F.R.C.S., M.R.C.O.G., hon. gynæcologist to the St. Marylebone and Western General Dispensary.

Examining Surgeons under the Factories Act, 1937: Dr. C. S. CARTER (Wollaston district, county of Northampton); Dr. R. N. PETRIE (Stromness district, county of Orkney).

Births, Marriages and Deaths

BIRTHS

CRESSWELL.—On March 17, at Dowlais, Glamorganshire, to the wife of Major P. E. Cresswell, R.A.M.C.—a daughter.

EARLAM.—On March 23, the wife of Dr. Francis Earlam, of Liverpool—a daughter.

MEADOWS.—On March 25, at Westminster Hospital, the wife of Dr. P. Meadows—a son.

MIMPRISS.—On March 18, at Esher, the wife of Mr. T. W. Mimpriss, F.R.C.S.—a son.

PARRY.—On March 18, at Ipswich, the wife of Dr. W. E. C. Parry—a son.

REID.—On March 26, at Colchester, the wife of Mr. R. W. Reid, F.R.C.S.—twin daughters.

ROBERTSON.—On March 19, at South Nutfield, the wife of Captain J. R. Robertson, R.A.M.C.—a son.

SAVAGE.—On March 19, at Brentwood, the wife of Surgeon Lieut.-Commander S. J. Savage, R.N.—a daughter.

TIERNEY.—On March 20, at Westcliff-on-Sea, the wife of Major T. F. Tierney, R.A.M.C.—a son.

MARRIAGES

MCGOWAN—BARCLAY.—On March 20, in Manchester, Graham Kemp McGowan, B.M., of Oldham, to Rosalind Storey Barclay, M.B., of Mobberley, Cheshire.

DEATHS

COOKE.—On March 23, at Hunstanton, Louisa Rosa Cooke, L.R.C.P.E.

FARNFIELD.—On March 24, at Sunningdale, William Walter Farnfield, M.R.C.S.

FEGEN.—On March 25, in Lambeth Hospital, Charles Milton Fegen, M.R.C.S., D.P.H., of Dunsfold, Surrey, aged 78.

FENNINGS.—On March 22, at Seaford, Arthur Allen Fennings, M.D. Durh.

HANSON.—On March 20, at Sketty, Swansea, Alfred Hanson, M.R.C.S.

HANSON.—On March 22, Reginald John Edward Hanson, O.B.E., M.B. Camb., Surgeon Captain, R.N.V.R., of Fowey, Cornwall, aged 69.

HEWER.—On March 24, at Glenthorne, Tarporley, Cheshire, Cecil Mackenzie Hewer, O.B.E., F.R.C.S.

LIGHT.—On March 24, Leonard William Light, M.R.C.S., of Southminster, Essex.

LYNCH.—On March 22, George William Augustus Lynch, M.B. Camb., of Aldeburgh, Suffolk, aged 78.

MAPOTHER.—On March 20, at Mill Hill Emergency Hospital, Edward Mapother, M.D. Lond., F.R.C.P., F.R.C.S., aged 58.

WHITE.—On March 25, at Harrow-on-the-Hill, John Douglas Campbell White, M.D. Camb., aged 68.

Vacancies

Arlesey, Three Counties Hosp.—Temp. asst. M.O., 8 guineas per week.

Barnsley, Beckett Hosp. and Dispensary.—Cas. O. and jun. H.S., £250 and £150 respectively.

Birmingham City.—Temp. senior asst. pathologist, 10 guineas per week.

Birkenhead County Borough.—Asst. school M.O. and asst. M.O.H., £500.

Bolton County Borough.—Temp. asst. M.O. for Townleys Hosp., at rate of £400.

Bradford Royal Infirmary.—H.P. to radium and skin dept., £200. Also H.S., at rate of £150.

British Postgraduate Medical School, Ducane Road, W.12.—Cas. O., at rate of £150.

Burton-on-Trent General Infirmary.—Cas. O. and H.P., £150.

Coventry, Coventry and Warwickshire Hosp.—Cas. O. and second H.S. to fracture and orthopædic dept., £150.

Derbyshire Royal Infirmary.—H.S. for cas. dept., £150.

Dudley, Guest Hosp.—Cas. H.S., £150.

Ealing, W.13. King Edward Memorial Hospital.—Res. M.O. £275. Also cas. O. and dep. res. M.O. at rate of £225.

Ealing Borough.—Asst. M.O., £450.

East Ham Memorial Hosp., Shrewsbury Road, E.7.—Temp. hon. radiologist, 3 guineas per session.

Hereford, Herefordshire General Hosp.—H.S. to cas. and ear, nose, and throat depts. and H.P. each £120.

Hull Corporation, Beverley Road Hosp.—Res. asst. M.O., also res. temp. asst. M.O., each £350.

Hull Royal Infirmary.—H.S. to ophth. and ear, nose, and throat depts., at rate of £150.

Islington Metropolitan Borough.—Temp. M.O. (A.R.P.), at rate of £550.

Kidderminster and District General Hosp.—Jun. H.S., at rate of £100.

Lancaster Royal Infirmary.—Orthopædic and cas. H.S., at rate of £130.

Liverpool, Bootle General Hosp.—Cas. O., at rate of £150.

Liphook, Hants, King George's Sanatorium for Sailors.—Asst. M.O., at rate of £200.

Manchester Monsall Hospital.—Jun. res. asst. M.O. at rate of £250.

Middlesbrough, North Riding Infirmary.—Cas. O., at rate of £150.

Nelson Hosp., Merton, S.W.20.—Two res. H.S.'s, each at rate of £200.

Newcastle-upon-Tyne Education Committee.—Asst. school M.O., £500.

Newport County Borough.—Temp. asst. M.O.H., at rate of £500. Also asst. res. M.O., at rate of £200.

Newport, Mon., Royal Gwent Hosp.—Cas. O., at rate of £175.

Northampton General Hosp.—Res. anæsthetist also H.S. to E.N. and T. dept., each at rate of £150.

Nottingham, City Isolation Hosp.—Res. M.O., at rate of £150–£250.

Oldham County Borough.—Res. obstet. officer for municipal hosp., £350. Also res. asst. M.O. for the municipal hosp., at rate of £200.

Oldham, Royal Infirmary.—Sen. H.S., at rate of £250. Also two H.S.'s, each at rate of £175.

Oxford University.—Philip Walker studentship in pathology, £300–£350.

Preston and County of Lancaster Queen Victoria Royal Infirmary. H.S. to eye, ear, nose, and throat depts., at rate of £150.

Rochdale Infirmary.—H.P., £150.

Rochdale Infirmary and Dispensary.—Second H.S., £150.

Salford, Hope Hospital.—Temp. res. obstet. O., £450.

Sheffield City.—Asst. tuber. officer for Winter Street Hosp., £350.

Stockport Infirmary.—Two H.S.'s to spec. depts., each at rate of £150.

Victoria Hosp. for Children, Tite Street, Chelsea, S.W.3.—H.P., at rate of £100.

Warwickshire and Coventry Joint Committee for Tuberculosis.—Jun. asst. M.O. for Memorial Sanatorium, at rate of £250.

Weir Hosp., Weir Road, Balham, S.W.12.—Jun. res. M.O., £150.

Weston-super-Mare Hosp.—Res. H.S., £150.

Winchester, Royal Hampshire County Hosp.—H.S., at rate of £100.

The Chief Inspector of Factories announces a vacant appointment for an examining surgeon at Horsham, Sussex.

Mr. Thomas Phillips's "Cheap Glory" (Harrap and Co. 1939. Pp. 283. 8*s.* 3*d.*) is the story of a world heavyweight boxing champion and his last fight, told by himself in vivid language. The hero has been warned by his doctor that he might become punch-drunk and blind. And indeed he gives a self-description of early symptoms—difficulties in concentration, remembering and clear thinking—which is well worth reading from the medical standpoint. Still, he is determined to fight once more and then retire. He wins after a dramatic fight, but he loses his eyesight. His own symptoms and some sketches of other battered figures of the ring illustrate well the problems of "punch-drunk," the psychological type of the pugilist who takes too much punishment, the symptoms of traumatic encephalopathy, and the psychological reaction to them. This is also an exciting story apart from its medical interest.

NOTES, COMMENTS AND ABSTRACTS

THE GREAT MACE OF THE ROYAL COLLEGE OF SURGEONS

IN 1801 the then Company of Surgeons resolved that "a staff for the Beadal was to be provided under the direction of the Master," and a club-shaped mace, such as is carried before ecclesiastical dignitaries in cathedrals, with a silver head bearing the arms used by the company before 1822 was selected; this is still preserved in the hall of the college. The great mace itself was presented to the college by King George IV in 1822 when he granted it a new charter changing the titles of master and governor to president and vice-president. From this time the court of assistants was styled the council of the college, and the mace as an emblem of authority has ever since been borne before the president and council and deposited on the table while they are in session. The mace has its origin in the heavy weapon carried by mailed knights in the thirteenth and fourteenth centuries which was a survival of the club of still earlier times. Maces of brass are mentioned in records as early as 1297 when they were regarded as a sceptre or staff of office and borne before certain officials. In the sixteenth century mace-bearers began to be appointed in corporate towns and boroughs.

The great mace of the college consists of a richly ornamented staff of silver, heavily gilded, surmounted by the Royal Crown of England and the British Arms under the canopy. The brackets supporting the head are in the shape of caryatides. The staff is engraved with the royal cypher G.R. and the national emblems, the rose, shamrock and thistle with leaves entwined, and a leaping horse with an acorn below it, a symbol of the House of Hanover. The date 1822 is followed by a Latin inscription commemorating the gift, and below the inscription the armorial bearings, crest, supporters and motto of the college are engraved. The mace was made by Rundell, Bridge and Rundell to King George's order and bears the name of Sir Everard Home the first president of the college. The knob or heel terminating the staff is the last survival of the old fighting weapon. The mace measures 4 ft. 4 in. in length and weighs 14 lb. 9 oz.

TIPS FOR THE YOUNG OFFICER

AN officer, combatant or medical, has much to learn when he first joins the army and in the last war he learnt a good deal of it by bitter experience, an experience that was the more bitter because it was learnt at the expense of his men rather than of himself. There is plenty of room, then, for guides written by the old hands that tell the young officer something of what he must know and help him to find out the rest. In his "Field Notes for Regimental Officers" (London: J. and A. Churchill. 1940, pp. 148. 3*s.* 6*d.*) Colonel E. M. Cowell supplies such a guide. An appendix, for instance, tells the newcomer to whom he should go for essential stores. It is possible to get anything in the army if you know where to go and how to set about it, but the same man will not necessarily supply rifle oil, waggon oil and castor oil. Not that it is really different from civilian life for no-one would expect to get all these from the same shop. The chapter on personal hygiene lays down that it is "the duty of the officer to see that these recommendations for cleanliness are carried out," a point that has lately been raised more than once in Parliament. Inexperienced officers are apt to think that the M.O. is responsible for this throughout the unit. On the other hand temporary officers of the R.A.M.C. do not always realise that they also have men under them for whom they are responsible, as is the platoon or section commander in the combatant units. The medical officer, says the preface of this book, should be more than a doctor—he is a soldier first, and an officer next. This is important to remember, for the new M.O. cannot see things from the professional soldier's point of view. One of the troubles of senior officers, too, is that many young men do not know what doctoring means. Their studies up to the time of qualification have been nine parts dealing with the sick, and one part or less prevention. As soon as they enter the army it is nine parts prevention and one part or less dealing with the sick. Keeping a thousand fit men fit is a form of clinical medicine and a very interesting one too. Even this is not the end of it. Young men on the strength of having done six months as a house-officer think they are already entitled to be specialists; and do not want to join up "until there is something to do." If they wait until there is a nicely-furnished pigeon-hole ready for them they will have to wait a long time and will not be much use when they get there. Colonel Cowell's little book will do something to explode this idea.

A STEAM INHALER.—With reference to the note on page 532 of our issue of March 16, Messrs. Burgess Products inform us that their vaporiser is dispatched fully assembled. All that the user has to do is to fill the jug with cold water to within an inch of the top, put a small piece of cotton-wool on the perforated disc, add the inhalant, put on the lid and switch on the current. It is not necessary to remove the unit from the jug unless the vaporiser is used only for continuous vaporisation of tincture of benzoin, and then only about once a month. Where a patient needs the vaporiser at night he will obtain relief quicker and with much less trouble than with the familiar kettle and jug method.

Medical Diary

Week beginning April 1

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1.

TUESDAY
Orthopædics—4.30 P.M., annual general meeting. Prof. Geoffrey Jefferson and Mr. W. J. Eastwood: Fractures and Dislocation of the Cervical Vertebræ.

WEDNESDAY
History of Medicine—2.30 P.M.—Mr. R. J. Forbes (Amsterdam): Im Hotep, The First Physician. Sir St Clair Thomson: (1) Engraved Portrait of a Centenarian, published 1806; (2) Engravings of The Drinking and Dipping Wells in Hyde Park, dated 1802. Sir Walter Langdon-Brown: Richard Mead's Harveian Oration.

FRIDAY
Epidemiology and State Medicine—3.30 P.M., Dr. J. A. Glover: Evacuation—Some Epidemiological Observations on the First Four Months. (Presidential address.)

BRITISH POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12.

MONDAY.—10 A.M., Mr. Watson Jones: Treatment of Fractures with special reference to War Conditions.

WEDNESDAY.—11.30 A.M., clinico-pathological conference (medical). 3 P.M., clinico-pathological conference (surgical).

THURSDAY.—2 P.M., Dr. Duncan White: radiological conference.

FRIDAY.—2 P.M., clinico-pathological conference (gynæcological). 2.30 P.M., Dr. C. M. Hinds Howell: ward clinic. 2.30 P.M., Mr. V. B. Green-Armytage: Sterility clinic.

DAILY.—10 A.M.–4 P.M., medical clinics; surgical clinics and operations; obstetrical and gynæcological clinics and operations. 1.30–2 P.M., post-mortem demonstration.

FELLOWSHIP OF MEDICINE AND POSTGRADUATE MEDICAL ASSOCIATION, 1, Wimpole Street W.1.

Medical Society of London, 11, Chandos Street, W.1. TUES., 5 P.M., Mr. Kenneth Heritage: Urethra, Testicle and Prostate. FRI., 5 P.M., Mr. J. Swift Joly: Kidney.—St. Mary's Hospital, Paddington, W.2. WED., 5.30 P.M., clinical class in F.R.C.S. course.—Brompton Hospital, S.W.3. TUES., 5.30 P.M., and THURS., 5 P.M., M.R.C.P. course in chest diseases.—Royal College of Surgeons, Lincoln's Inn Fields, W.C.2. WED., 3.30 P.M., and THURS., 3 P.M., F.R.C.S. pathology course.—Royal National Orthopædic Hospital, Brockley Hill, Stanmore. FRI., 2 P.M., F.R.C.S. orthopædic course.—Royal Cancer Hospital, Fulham Road, S.W.3. MON. to SAT., 9.30 A.M., Course for F.R.C.S. (final).